Access DB# 42773

SEARCH REQUEST FORM

Scientific and Technical Information Center

mcj

Requester's Full Name: Natalie Davis Examiner #: 78462 Date: 5-21-01
Art Unit: 1642 Phone Number 308-6410 Serial Number: 09/622035
Mail Box and Bldg/Room Location: 8E12 / CM1 9B09 Results Format Preferred (circle): (PAPER) DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

Earliest Priority Filing Date: 2-26-98

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search for a cancer vaccine comprising a polypeptide of the COS5 family or of the 791Tgp72 antigen OR the 791Tgp72 antigen in a pharmaceutical composition.

See claim 1, 2, 22

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Online Time: 22

Type of Search

NA Sequence (#) _____
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Vendors and cost where applicable

STN _____
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PTO-1590 (1-2000)

Davis, N.
09/623035

(FILE 'CAPLUS' ENTERED AT 10:40:55 ON 01 JUN 2001)

L3 208 SEA FILE=CAPLUS ABB=ON PLU=ON (CD55 OR CD 55)(S)(POLYPEPTIDE OR POLYPROTEIN OR PEPTIDE OR PROTEIN) OR 791T?(S)ANTIGEN

L4 65 SEA FILE=CAPLUS ABB=ON PLU=ON L3 AND (?CANCER? OR ?CARCIN? OR ?TUMOUR? OR ?TUMOR? OR ?NEOPLAS?)

L5 10 SEA FILE=CAPLUS ABB=ON PLU=ON L4 AND (VACCIN? OR IMMUNIZ? OR IMMUNIS?)

L1 410 SEA FILE=CAPLUS ABB=ON PLU=ON CD55 OR CD 55 OR 791T?

L2 116 SEA FILE=CAPLUS ABB=ON PLU=ON L1 AND (?CANCER? OR ?CARCIN? OR ?TUMOUR? OR ?TUMOR? OR ?NEOPLAS?)

L7 13 SEA FILE=CAPLUS ABB=ON PLU=ON L2 AND (VACCIN? OR IMMUNIZ? OR IMMUNIS?)

L8 13 L5 OR L7

L8 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:98150 CAPLUS

TITLE: **CD55** is over-expressed in the **tumour** environment

AUTHOR(S): Li, L.; Spendlove, I.; Morgan, J.; Durrant, L. G.

CORPORATE SOURCE: CRC Academic Unit of Clinical Oncology, University of Nottingham, Nottingham, NG5 1PB, UK

SOURCE: Br. J. Cancer (2001), 84(1), 80-86
CODEN: BJCAAI; ISSN: 0007-0920

PUBLISHER: Harcourt Publishers Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **CD55** is a **protein** that protects cells from complement-mediated attack. **791Tgp72** is an **antigen** which has been used succesfully as a target for both **tumor** imaging and **cancer vaccines**. **791Tgp72** has recently been identified as **CD55**. Quant. expression of **CD55** in the **tumor** environment was therefore studied. **Tumor** cells showed a 4-100-fold increase in **CD55** cell surface expression when compared to normal cells. Immunohistochem. staining of colorectal **tumors** also revealed high expression of **CD55** in the stroma. To examine the source of this stromal **CD55** the ability of both epithelial cells and endothelial cells to produce extracellular **CD55** was measured. **Tumor** cell lines deposit **CD55** into their extracellular matrix (ECM) in direct proportion to their cell surface expression. In contrast the ECM from HUVEC cells contained large amts. of **CD55** despite expressing low levels of **CD55** on

their cell surface. Furthermore expression of **CD55** on HUVEC cells was increased by exposure to VEGF. Although it remains unclear why **CD55** is upregulated in the **tumor** environment its high level of expression on **tumor** cells and assocd. endothelium may explain why it is a good target for both imaging and immunotherapy.

REFERENCE COUNT: 29

REFERENCE(S):
(3) Austin, E; Immunol 1989, V67, P525 CAPLUS
(5) Collard, C; Circulation 1997, V96, P326 CAPLUS
(6) Coyne, K; J of Immunol 1992, V149, P2906 CAPLUS
(8) Durrant, L; Cancer Res 1994, V54, P4837 CAPLUS
(10) Durrant, L; Int J Cancer 2000, V85, P87 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:776817 CAPLUS

DOCUMENT NUMBER: 134:55263

TITLE: A therapeutic human anti-idiotypic antibody mimics **CD55** in three distinct regions

AUTHOR(S): Spendlove, Ian; Li, Li; Potter, Vanessa; Christiansen, Dale; Loveland, Bruce E.; Durrant, Lindy G.

CORPORATE SOURCE: CRC Academic Unit of Clinical Oncology, City Hospital, University of Nottingham, Nottingham, UK

SOURCE: Eur. J. Immunol. (2000), 30(10), 2944-2953
CODEN: EJIMAF; ISSN: 0014-2980

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The human anti-idiotypic antibody 105AD7 was isolated from a colorectal **cancer** patient receiving the anti-**tumor** antibody **791T**/36 for radioimmuno-scintigraphy of liver metastases. We have mapped the binding site of **791T**/36 to the first two small consensus repeat (SCR) domains of the complement regulatory **protein** (**CD55**) that is overexpressed by a wide range of solid **tumors**. Cloning of both antigen and anti-idiotype has identified the mol. basis of their mimicry. Amino acid homol. has been identified between three complementarity-detg. regions of 105AD7 and three regions of **CD55** within the first two SCR domains. **791T**/36 and anti-anti-idiotypic (Ab3) polyclonal antibodies raised against 105AD7 showed specific binding to these peptides. The antibodies were also found to bind synergistically to combinations of these

peptides, indicating cooperativity between the peptides in stabilizing antibody binding. This also implies that the contact face on both **CD55** antigen and 105AD7 is generated by the cooperation of several **peptides** positioned on two domains in each **protein**. Thus a human monoclonal anti-idiotypic antibody generated by a **cancer** patient is able to show both amino acid and structural homol. with the complement regulatory **protein CD55**. These findings help identify the mechanism by which a human anti-idiotypic antibody is able to mimic a **tumor**-assocd. antigen and stimulate anti-**tumor** B and T cell responses.

REFERENCE COUNT: 41

REFERENCE(S):
(1) Amin, S; Cancer Res 2000, V60, P3132 CAPLUS
(4) Austin, E; Immunology 1989, V67, P525 CAPLUS
(6) Azuma, A; Scand J Immunol 1995, V42, P202 CAPLUS
(7) Barlow, P; J Mol Biol 1993, V232, P268 CAPLUS
(8) Bentley, G; Nature 1990, V348, P254 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:162729 CAPLUS

DOCUMENT NUMBER: 132:306999

TITLE: A neoadjuvant clinical trial in colorectal **cancer** patients of the human anti-idiotypic antibody 105AD7, which mimics **CD55**

AUTHOR(S): Durrant, Lindy G.; Maxwell-Armstrong, Charles; Buckley, Declan; Amin, Schwann; Robins, R. Adrian; Carmichael, James; Scholefield, John H.

CORPORATE SOURCE: Cancer Research Campaign Academic Unit of Clinical Oncology, University of Nottingham, Nottingham, NG5 1PB, UK

SOURCE: Clin. Cancer Res. (2000), 6(2), 422-430
CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Thirty-five patients received 105AD7 human anti-idio-type **vaccination** prior to surgery for colorectal **carcinoma**. Patients were **immunized** before and also received one to two **immunizations** after surgical resection of their colorectal **cancer**. The **vaccine** was well tolerated with no assocd. toxicity. Lymphocytic infiltration within the resected **tumors** was quantified by immunohistochem. and image anal. Enhanced infiltration of helper T cells (CD4) and natural killer (NK) cells (CD56) were obsd. in the

tumors from **immunized** patients when compared with **tumors** from stage, grade, site, age, and sex matched unimmunized patients. NK activity was increased in the blood, peaking 7-10 days post **immunization** and then dropping rapidly and correlating with NK extravasation within the **tumor**. Comparison of the amino acid sequences of 105AD7 anti-idiotype and the antigen it mimics, **CD55**, has predicted that patients with HLA-DR1, HLA-DR3, and HLA-DR7 haplotypes should show helper T cell responses following 105AD7 **vaccination**. Eighty-three percent of patients expressing these haplotypes responded to 105AD7, whereas 88% of patients who failed to express these haplotypes were nonresponders. With a median follow-up of 4 yr (range, 2.5-6 yr) 65% of patients remained disease free. This trial shows that 105AD7 stimulates **antitumor** inflammatory responses allowing extravasation within **tumor** deposits of both helper T cells and NK cells. This represents a way of evaluating immune responses in patients both within the blood and at the **tumor** site. The study confirms that **immunization** with a human anti-idiotypic antibody results in immune responses in 83% of patients with a permissive haplotype.

REFERENCE COUNT: 25

REFERENCE(S):
(1) Austin, E; Immunology 1989, V67, P525 CAPLUS
(3) Chatterjee, S; Cancer Res 1998, V58, P1217 CAPLUS
(7) Durrant, L; Int J Cancer 1995, V61, P62 CAPLUS
(8) Durrant, L; Int J Cancer 1995, V61, P62 CAPLUS
(9) Durrant, L; Int J Cancer 2000, V85, P87 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:14224 CAPLUS

DOCUMENT NUMBER: 132:48781

TITLE: 105AD7 **cancer vaccine** stimulates anti-**tumor** helper and cytotoxic T-cell responses in colorectal **cancer** patients but repeated **immunizations** are required to maintain these responses

AUTHOR(S): Durrant, Lindy G.; Buckley, Declan J.; Robins, R. Adrian; Spendlove, Ian

CORPORATE SOURCE: CRC Department of Clinical Oncology, University of Nottingham, Nottingham, NG5 1PB, UK

SOURCE: Int. J. Cancer (2000), 85(1), 87-92
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 105AD7 is a human anti-idiotypic antibody that recognizes the binding site of the anti-**tumor** antibody **791T**/36 and can thereby mimic the **CD55 antigen**. The mol. basis of 105AD7 mimicry has been identified with 3 CDR regions of 105AD7 showing similarity to 3 regions of **CD55**. These regions have been analyzed for potential T-cell epitopes, and sequences that are predicted to bind to HLA/A1,3,24 and to HLA/DR1,3,7 have been identified within the CDRH3 region of 105AD7. These epitopes should be stimulating CD8 and CD4 responses, resp. This prediction was tested on 12 colorectal **cancer** patients receiving 105AD7 therapy. There was good concordance in 10 of 11 patients between accumulation of CD8RO cells or **tumor** killing and expression of HLA/A1,3,24. The only patient who failed to respond had a non-permissive class II haplotype and failed to show a helper response. Again 10 of 11 patients showing accumulation of CD4RO cells, in vitro blastogenesis responses, enhanced IL-2 or enhanced NK activity expressed one or more of the HLA/DR1,3,7 haplotypes. Although there was a consistent accumulation of CD45RO cells following 14 of 18 **immunizations**, only one patient showed a sustained memory response. Our results suggest that 105AD7 can stimulate CD4 and CD8 responses in patients with the appropriate haplotype. However, it may be necessary to continue to **immunize**, since few patients produce a sustained memory response.

REFERENCE COUNT: 21
REFERENCE(S):
(1) Akbar, A; J Immunol 1988, V140, P2171 CAPLUS
(5) Brusic, V; Nucleic Acids Res 1997, V25, P269 CAPLUS
(7) Durrant, L; Cancer Res 1994, V54, P4837 CAPLUS
(9) McMichael, A; J exp Med 1998, V187, P1367 CAPLUS
(10) Parker, K; J Immunol 1994, V152, P163 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:566166 CAPLUS
DOCUMENT NUMBER: 131:183869
TITLE: Purification, cDNA cloning, and properties of human **tumor**-associated **antigen** **791Tgp72**
INVENTOR(S): Durrant, Linda Gillian; Spendlove, Ian
PATENT ASSIGNEE(S): Cancer Research Campaign Technology Limited, UK
SOURCE: PCT Int. Appl., 84 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943800	A1	19990902	WO 1999-GB582	19990226
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9926330	A1	19990915	AU 1999-26330	19990226
EP 1056851	A1	20001206	EP 1999-906367	19990226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: GB 1998-4065 A 19980226
WO 1999-GB582 W 19990226

AB Previous attempts to purify and identify the **791Tgp72 antigen** using both immunopptn. and affinity chromatog. have failed due to poor yields and the conformational dependence of antibody **791T**/36 for **antigen** binding. A modified method of affinity purifn. of **791Tgp72** is provided which has led to the isolation of this **antigen**. Biotinylation of cell membranes allows optimization of the purifn. protocol, enabling efficient tracing of purified fractions. Use of the mild detergent octyl glucoside and the introduction of an ultracentrifugation step has enhanced the purifn. 50-100-fold. The affinity chromatog. has significantly been improved by covalently coupling the capturing antibody (**791T**/36) to protein A-Sepharose. Over 100 .mu.g of the antigen was purified and N-terminal sequencing identified the mol as being a member of the C55/decay accelerating factor family. Further sequencing has revealed that the coding region of **791Tgp72** cDNA is the same as that for a known **CD55 protein**. There are, however, differences between the **791Tgp72** and **CD55 proteins**, for example in the glycosylation pattern of the mols. **Cancer vaccines** comprising a **polypeptide** of the **CD55** family, or fragments or derivs. of **polypeptides** of the **CD55** family, are thus provided.

REFERENCE COUNT: 8

REFERENCE(S): (1) Biovation Limited; WO 9833523 A 1998 CAPLUS
(2) Cancer Res Campaign Tech; WO 9732021 A 1997 CAPLUS
(3) Caras, I; Nature 1987, V325, P545 CAPLUS
(4) Durrant, L; Anti-Cancer Drugs 1997, V8(8), P727 CAPLUS
(5) Juhl, H; Journal of Surgical Oncology 1997, V64(3), P222 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:348353 CAPLUS
DOCUMENT NUMBER: 131:128815
TITLE: Decay accelerating factor (**CD55**): a target for **cancer vaccines**?
AUTHOR(S): Spendlove, Ian; Li, Li; Carmichael, James; Durrant, Lindy G.
CORPORATE SOURCE: Cancer Research Campaign Academic Unit of Clinical Oncology, City Hospital, University of Nottingham, Nottingham, NG5 IPB, UK
SOURCE: Cancer Res. (1999), 59(10), 2282-2286
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **791Tgp72 antigen** has been used successfully as a target for **tumor** imaging and T-cell immunotherapy. We have characterized this **antigen** using the monoclonal antibody **791T**/36 as a 72/66 kDa doublet. NH2-terminal **protein** sequencing of the two bands revealed identity with the complement regulatory **protein CD55**. Antibodies recognizing different domains of **CD55** were also shown to bind to the purified **791Tgp72**, although sequence anal. of the cDNA cloned from **791T tumor** cells showed 100% homol. with **CD55** and transfection of the cDNA into **antigen**-neg. CHO cells resulted in binding of **791T**/36. This identifies the **tumor antigen 791Tgp72** as **CD55**. This protein protects cells from complement attack; however, it can also transduce signals in lymphocytes and is a ligand for CD97, expressed by activated T cells. These results suggest that **CD55** plays a roll in signaling between the innate and adaptive immune responses. It is therefore a very intriguing target, because absence of the mol. makes the **tumor** cells susceptible to complement, whereas protective overexpression results in the antigen being a target for T-cell immunotherapy.
REFERENCE COUNT: 30
REFERENCE(S): (1) Altschul, S; J Mol Biol 1990, V215, P403

CAPLUS
(3) Austin, E; Immunology 1989, V67, P525 CAPLUS
(7) Chatterjee, S; Cancer Res 1998, V58, P1217 CAPLUS
(8) Coyne, K; J Immunol 1992, V149, P2906 CAPLUS
(9) Davis, L; J Immunol 1988, V141, P2246 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:544220 CAPLUS
DOCUMENT NUMBER: 123:167380
TITLE: Induction of cellular immune responses by a murine monoclonal anti-idiotypic antibody recognizing the **791Tgp72** **antigen** expressed on colorectal, gastric and ovarian human **tumors**
AUTHOR(S): Durrant, Lindy G.; Doran, Mark; Austin, Eric B.; Robins, R. Adrian
CORPORATE SOURCE: Department Surgery, University of Nottingham, Nottingham, UK
SOURCE: Int. J. Cancer (1995), 61(1), 62-6
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English

AB There is accumulating evidence that cellular rather than antibody responses are more effective for **tumor** rejection. It is therefore important to screen anti-idiotypic (anti-id) antibodies for their ability to stimulate anti-**tumor** T-cell responses. The human anti-id monoclonal antibody (MAb) 105AD7 stimulated both delayed-type hypersensitivity (DTH) responses in animals and antigen-specific blastogenesis and IL-2 induction in advanced **cancer** patients. It may not be necessary to use human anti-id antibodies as murine anti-id antibodies, which elicit DTH responses against immunodominant human T-cell epitopes and may be just as useful in the clinic. We have therefore produced a murine anti-id antibody to the same MAb as was used to generate the human anti-id antibody and screened it for its ability to generate cellular anti-**tumor** immune responses. Low-dose **immunization** with the murine anti-id MAb NCRC60, which recognizes the paratope of the anti-**791Tgp72** MAb **791T**/36, induced DTH responses to **791Tgp72** -expressing **tumor** cells but not to **antigen**-neg. cells. DTH responses with no detectable antibody responses were induced with 5 .mu.g of anti-id NCRC60 without adjuvant. Addn. of either complete Freund's adjuvant or Quil A did not enhance DTH responses. However, when the anti-id NCRC60 was linked to KLH and injected in the presence of Freund's adjuvant antianti-id antibodies and anti-**791Tgp72** antibodies were induced. NCRC60 anti-id

was also capable in vitro of priming human T cells from **cancer** patients to proliferate in response to secondary stimulation with **791Tgp72**-expressing **tumor** cells, suggesting that it may have therapeutic potential in **cancer** patients.

L8 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:609563 CAPLUS
DOCUMENT NUMBER: 113:209563
TITLE: Syngeneic anti-idiotypic antibody prevents localization of a murine monoclonal antibody in human **tumor** xenografts
AUTHOR(S): Pimm, Malcolm V.; Baldwin, Robert W.
CORPORATE SOURCE: Cancer Res. Campaign, Univ. Nottingham, Nottingham, NG7 2RD, UK
SOURCE: Eur. J. Cancer (1990), 26(5), 567-8
CODEN: EJCAEL
DOCUMENT TYPE: Journal
LANGUAGE: English
AB BALB/c mice were **immunized** against syngeneic mouse monoclonal antibody (Mab) **791T**/36 to produce anti-idiotypic antibody. To examine the effect of this antibody on **tumor** localization of the Mab, serum from these mice was transferred to nude mice with human **tumor** xenografts and distribution was studied with I-125 labeled Mab. Serum contg. anti-idiotypic antibody prevented **tumor** localization of the Mab. This finding has implications for the clin. use of human or humanized Mab since, if these evoke anti-idiotypic antibody, this alone may be sufficient to prevent **tumor** targeting.

L8 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:452149 CAPLUS
DOCUMENT NUMBER: 113:52149
TITLE: A bispecific monoclonal antibody against methotrexate and a human **tumor** associated antigen augments cytotoxicity of methotrexate-carrier conjugate
AUTHOR(S): Pimm, M. V.; Robins, R. A.; Embleton, M. J.; Jacobs, E.; Markham, A. J.; Charleston, A.; Baldwin, R. W.
CORPORATE SOURCE: Cancer Res. Campaign Lab., Univ. Nottingham, Nottingham, NG7 2RD, UK
SOURCE: Br. J. Cancer (1990), 61(4), 508-13
CODEN: BJCAAI; ISSN: 0007-0920
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A bispecific monoclonal antibody, reactive with methotrexate (MTX) and a **tumor** assocd. **antigen** (gp72), has been

produced by fusing spleen cells from MTX **immunized** mice with **791T**/36/3 (anti-gp72) hybridoma. The hybrid antibody was purified from anti-MTX and anti-gp72 antibodies present in the hybridoma culture supernatant by combinations of affinity chromatog. on a MTX-agarose immunoabsorbent and stepwise acid elution from Sepharose-Protein A. A particular feature of the present antibody is that it reacts with conjugated MTX; this would allow in vivo-targeting of conjugates, increasing many fold the no. of mols. of drug carried or localizing to pre-targeted antibody. Dual binding between **tumor** cell surface antigen and MTX was demonstrated by the ability of the hybrid antibody to bridge between **tumor** cells and MTX as MTX-HSA conjugate, reaction here being detected by flow cytofluorimetry. Purified hybrid antibody specifically enhanced the in vitro cytotoxicity of MTX-HSA for gp72 pos. **tumor** cells.

L8 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:513396 CAPLUS
DOCUMENT NUMBER: 111:113396
TITLE: Human monoclonal anti-idiotypic antibody to the **tumor**-associated antibody **791T**/36
AUTHOR(S): Austin, E. B.; Robins, R. A.; Durrant, L. G.; Price, M. R.; Baldwin, R. W.
CORPORATE SOURCE: Cancer Res. Campaign Lab., Univ. Nottingham, Nottingham, NG7 2RD, UK
SOURCE: Immunology (1989), 67(4), 525-30
CODEN: IMMUAM; ISSN: 0019-2805
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A human monoclonal antibody, 105AD7, was produced by fusion of a mouse/human heteromyeloma cell line with lymphocytes from a patient previously injected with mouse monoclonal antibody **791T**/36 for **tumor** immunoscintigraphy. The 105AD7 hybridoma has been in continuous culture for >12 mo, producing a human monoclonal IgG1 which binds to **791T**/36 (IgG2b) and its IgG2a class switch variant, but not a range of other monoclonal mouse Igs. In quant. flow cytometric assays, 105AD7 was shown to block the binding of fluorescein-labeled **791T**/36 to its target gp72 **antigen** at the surface of **tumor** cells, but not the binding of 228, an **anticarcinoembryonic antigen** (CEA) monoclonal antibody to CEA. Tests with purified 105AD7 antibody demonstrated a stoichiometric high-affinity interaction between 105AD7 and **791T**/36. Thus, 105AD7 is a human anti-idiotypic antibody which binds at or very close to the binding site of **791T**/36, and as such is a candidate for anti-idiotypic **immunization** of **cancer** patients.

L8 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:542587 CAPLUS
DOCUMENT NUMBER: 109:142587
TITLE: Cytotoxic conjugates of ribosome-inhibiting proteins with antibodies, compositions and kits containing them, and their use
INVENTOR(S): Scannon, Patrick J.; Baldwin, Robert William; Byers, Vera S.
PATENT ASSIGNEE(S): Xoma Corp., USA
SOURCE: Eur. Pat. Appl., 87 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 256471	A2	19880224	EP 1987-111540	19870810
EP 256471	A3	19891025		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 63115826	A2	19880520	JP 1987-203363	19870815

PRIORITY APPLN. INFO.: US 1986-896999 19860815

AB An antibody to either a 72-kilodalton **tumor**-assocd. glycoprotein antigen (gp72) or **carcinoembryonic** antigen is conjugated to a ribosome-inhibiting protein for use as a cytotoxic agent for treatment of **cancers** such as colorectal **carcinoma**, ovarian **carcinoma**, and osteogenic sarcoma. Mice were **immunized** with cultured human **791T** osteogenic sarcoma cells, and spleen cells from the mice were fused with mice myeloma cells. Hybridoma XMNCO-791 was isolated which produced an IgG2b monoclonal antibody binding to colorectal and ovarian **carcinoma** and osteogenic sarcoma cells. This antibody showed complement-mediated cytotoxicity towards osteogenic sarcoma, prostate **carcinoma**, and HeLa cells in vitro. When injected into humans, the 131I-labeled antibody localized selectively in primary and metastatic colon **cancers**. Extn. of the labeled material from resected colon tissue revealed that the antibody bound to a 72-kilodalton glycoprotein **antigen** identical to gp72 on **791T** cells. The antibody was conjugated to ricin A chain by use of N-succinimidyl 3-(2-pyridyldithio)propionate. The conjugate specifically killed **tumor** cells expressing gp72 in vitro and was effective in vivo against human osteogenic sarcoma **791T** xenografts in mice (8 doses of 12 mg/kg i.p. at 2-3-day intervals).

L8 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1984:528545 CAPLUS
DOCUMENT NUMBER: 101:128545
TITLE: Analysis of a human osteogenic sarcoma antigen and its expression on various human **tumor** cell lines
AUTHOR(S): Campbell, D. G.; Price, M. R.; Baldwin, R. W.
CORPORATE SOURCE: Cancer Res. Campaign Lab., Univ. Nottingham, Nottingham, NG7 2RD, UK
SOURCE: Int. J. Cancer (1984), 34(1), 31-7
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The murine monoclonal antibody **791T**/36 cross-reacts with cells other than the **immunizing** osteogenic sarcoma cell line **791T**, upon which the **791T**/36-defined epitope is expressed on a protein of apparent mol. wt. 72,000. An investigation was performed to det. whether the epitope occurred on similar mols. on other cell lines. Radiolabeled immunoppts., prepd. with the **791T**/36 antibody, from 3 osteogenic sarcoma cell lines (2 OS, 788T, and 278T), the prostate **carcinoma** EB33, and the colon **carcinoma** HcLo, each contained a protein with a mol. wt. of 72,000 as the major constituent, together with, in some cases, material of lower mol. wt. This heterogeneity was shown by neuraminidase treatment of the immune ppts. to be due to variations in sialic acid content of the antigens since, in 5 of the 6 cell lines tested, such treatment produced homogeneous material of apparent mol. wt. 55,000. Chymotrypsin treatment of the immune ppts. produced in each instance a major polypeptide of mol. wt. 47,000 which displayed no microheterogeneity. Immunoadsorbent-purified **antigen** from **791T** cells was shown to bind strongly to Sepharose-wheat-germ agglutinin and less to Sepharose-concanavalin A, confirming the glycoprotein nature of this **antigen**. These studies demonstrate that mols. expressing the **791T**/36-defined epitopes on different **tumor** cell lines are glycoproteins which display heterogeneity with respect to apparent mol. wt. that is attributable to varying degrees of sialylation. No apparent differences were detected in the polypeptide backbone of these antigenic mols.

L8 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1981:495310 CAPLUS
DOCUMENT NUMBER: 95:95310
TITLE: **Antitumor** reactions of monoclonal antibody against a human osteogenic-sarcoma cell line
AUTHOR(S): Embleton, M. J.; Gunn, B.; Byers, V. S.; Baldwin, R. W.
CORPORATE SOURCE: Cancer Res. Campaign Lab., Univ. Nottingham,

Nottingham, NG7 2RD, Engl.
SOURCE: Br. J. Cancer (1981), 43(5), 582-7
CODEN: BJCAAI; ISSN: 0007-0920
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Monoclonal antibody against an osteogenic-sarcoma cell line (**791T**) was prepd. by prodn. and cloning of a somatic cell hybrid between mouse myeloma P3-NS1 and spleen cells from **791T-immunized** mice. Three clones of a hybridoma producing antibody against **791T** had identical activity against a range of normal and **tumor** cell targets, reacting strongly against **791T** cells and another osteogenic sarcoma, 788T, and more weakly against a further 2 of a total of 10 osteogenic sarcoma lines. The antibody was neg. for fibroblasts from the donor of **791T** and for other fibroblasts, human red cells and peripheral mononuclear cells, and sheep red cells. It reacted against cell lines derived from **carcinomas** of the colon, lungs, bladder, and cervix. The antibody apparently reacts with a **tumor**-assocd. antigen expressed randomly on different **tumor** types, rather than specifically on osteogenic sarcomas.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, CANCERLIT' ENTERED AT 10:54:59 ON 01 JUN 2001)
L9 111 S L8
L10 38 DUP REM L9 (73 DUPLICATES REMOVED)

L10 ANSWER 1 OF 38 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001218007 MEDLINE
DOCUMENT NUMBER: 21186128 PubMed ID: 11291080
TITLE: Human anti-idiotypic antibodies can be good immunogens as they target FC receptors on antigen-presenting cells allowing efficient stimulation of both helper and cytotoxic T-cell responses.
AUTHOR: Durrant L G; Parsons T; Moss R; Spendlove I; Carter G; Carr F
CORPORATE SOURCE: CRC Academic Unit of Clinical Oncology, University of Nottingham, City Hospital, Nottingham, United Kingdom.. lindy.durrant@nottingham.ac.uk
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (2001 May 1) 92 (3) 414-20.
Journal code: GQU; 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104

ENTRY DATE: Entered STN: 20010425
Last Updated on STN: 20010425
Entered PubMed: 20010406
Entered Medline: 20010419

AB Anti-idiotypic antibodies that mimic **tumour**-associated antigens can stimulate anti-**tumour** T-cell responses. In this article, we have studied the role of Fc in the presentation of T-cell epitopes by 2 anti-idiotypic antibodies, 105AD7 and 708. The human monoclonal antibody 105AD7, which mimics **CD55**, stimulated strong in vitro T-cell proliferation, gammaIFN secretion and redirected cytotoxicity in unprimed T cells from healthy donors. However, removal of the Fc region of the anti-idiotype reduced the sensitivity of the assay 1,000-fold, as did inhibiting Fc uptake of the anti-idiotype by an excess of human IgG. The mouse anti-idiotype 708, which mimics CEA, failed to stimulate in vitro T-cell responses on unprimed T cells from healthy donors. However, when a human IgG1 Fc region replaced its mouse Fc region, the anti-idiotype induced T-cell proliferation, gammaIFN secretion and redirected cytotoxicity in lymphocytes from unimmunised donors. Human anti-idiotypes are therefore good immunogens since they target Fc receptors on antigen-presenting cells, allowing efficient stimulation of both helper and cytotoxic T-cell responses. The immunogenicity of other anti-idiotypes may therefore be enhanced by human Fc targeting of antigen-presenting cells. Copyright 2001 Wiley-Liss, Inc.

L10 ANSWER 2 OF 38 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001108881 MEDLINE
DOCUMENT NUMBER: 21066118 PubMed ID: 11139317
TITLE: **CD55** is over-expressed in the **tumour** environment.
AUTHOR: Li L; Spendlove I; Morgan J; Durrant L G
CORPORATE SOURCE: CRC Academic Unit of Clinical Oncology, University of Nottingham, City Hospital, Hucknall Road, Nottingham, NG5 1PB, UK.
SOURCE: BRITISH JOURNAL OF CANCER, (2001 Jan 5) 84 (1) 80-6.
Journal code: AV4. ISSN: 0007-0920.
PUB. COUNTRY: Scotland: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered PubMed: 20010126
Entered Medline: 20010208

AB **CD55** is a **protein** that protects cells from complement-mediated attack. **791Tgp72** is an **antigen** which has been used successfully as a target for both **tumour**

imaging and **cancer vaccines**. **791Tgp72** has recently been identified as **CD55**. Quantitative expression of **CD55** in the **tumour** environment was therefore studied. **Tumour** cells showed a 4-100-fold increase in **CD55** cell surface expression when compared to normal cells. Immunohistochemical staining of colorectal **tumours** also revealed high expression of **CD55** in the stroma. To examine the source of this stromal **CD55** the ability of both epithelial cells and endothelial cells to produce extracellular **CD55** was measured. **Tumour** cell lines deposit **CD55** into their extracellular matrix (ECM) in direct proportion to their cell surface expression. In contrast the ECM from HUVEC cells contained large amounts of **CD55** despite expressing low levels of **CD55** on their cell surface. Furthermore expression of **CD55** on HUVEC cells was increased by exposure to VEGF. Although it remains unclear why **CD55** is upregulated in the **tumour** environment its high level of expression on **tumour** cells and associated endothelium may explain why it is a good target for both imaging and immunotherapy. Copyright 2001 **Cancer** Research Campaign.

L10 ANSWER 3 OF 38 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-349917 [30] WPIDS
DOC. NO. CPI: C2000-106406
TITLE: Inducing immune responses to weakly immunogenic, **tumor** associated peptide antigens for the treatment of breast and prostate **cancer**.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): BIRK, P; DALUM, I; GAUTAM, A; HAANING, J; KARLSSON, G; LEACH, D; MOURITSEN, S; NIELSEN, K G; STEINAA, L
PATENT ASSIGNEE(S): (MEBI-N) M & E BIOTECH AS
COUNTRY COUNT: 89
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000020027	A2	20000413	(200030)*	EN	219
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9958510	A	20000426	(200036)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 2000020027	A2	WO 1999-DK525	19991005
AU 9958510	A	AU 1999-58510	19991005

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9958510	A	Based on	WO 200020027

PRIORITY APPLN. INFO: US 1998-105011 19981020; DK 1998-1261 19981005

AN 2000-349917 [30] WPIDS

AB WO 200020027 A UPAB: 20000624

NOVELTY - A method (I) for inducing immune responses against weakly immunogenic cell-associated peptide antigens (PA) such as those associated with **cancers** (i.e. self-proteins) (e.g. human PSM (undefined), Her2 and/or fibroblast growth factor (FGF) 8b), is new.

DETAILED DESCRIPTION - A method (I) for inducing an immune responses against weakly immunogenic or non-immunogenic polypeptide antigens (PAs) in animals (including humans), comprising effecting simultaneous presentation by antigen producing cells (APCs) of the animals immune system of:

(1) at least 1 CTL (cytotoxic T-lymphocyte) group derived from the PA and/or at least 1 B-cell group derived from the cell-associated PA; and

(2) at least 1 first T helper cell group (TH1 group) which is foreign to the animal.

INDEPENDENT CLAIMS are also included for the following:

(1) a method (II) for the selection of an immunogenic analog of a cell-associated PA that is weakly immunogenic or non-immunogenic which is capable of inducing an immune response in an animal against cell displaying MHC (major histocompatability complex) Class I (MHC-I) molecules bound to group derived from the cell-associated PA, comprising:

(A) identifying a subsequence of the amino acid sequence of the cell-associated PA which does not contain known or predicted CTL groups;

(B) preparing at least 1 punitively immunogenic analogs of the PA by introducing at least 1 TH group foreign to the animal in a position within the subsequence identified in step (A); and

(C) selecting those analogs from step (B) which are verifiably capable of inducing a CTL response in the animal

(2) a method (III) for the preparation of a cell that produces analogs of cell-associated PAs, comprising introducing a nucleic acid encoding the analog into a vector and transforming a suitable host cell (III) with the vector;

(3) a method (IV) for preparing analogs of cell-associated PAs comprising culturing the transformed host cell (III) under conditions suitable for expression of the protein and recovering the PA analog from the culture;

(4) an analog (V) of human PSM (undefined) that is immunogenic in humans and comprises at least part of all known and predicted CTL and B-cell groups of PSM and includes at least 1 foreign TH group;

(5) an analog (VI) of Her2 that is immunogenic in humans and comprises at least part of all known and predicted CTL and B-cell groups of Her2 and includes at least 1 foreign TH group;

(6) an analog (VII) of human/murine FGF (fibroblast growth factor) 8b that is immunogenic in humans and comprises at least part of all known and predicted CTL and B-cell groups of FGF 8b and includes at least 1 foreign TH group;

(7) compositions comprising (V), (VI) and/or (VII) and an adjuvant;

(8) nucleic acids ((VIII)-(X)) encoding (V), (VI) and/or (VII);

(9) vectors ((XI)-(XIII)) comprising (VIII)-(X) (respectively);

(10) a transformed cell (XIV) comprising (XI)-(XIII);

(11) compositions for inducing production of antibodies against PSM, Her2 and FGF 8b, comprising (VIII)-(X) and/or (XI)-(XIII) and an adjuvant; and

(12) a method for the preparation of the cell (XIV), comprising transforming a host cell with (VIII)-(X) or (XI)-(XIII).

USE - (I) is used to stimulate immune responses to weakly, or non-immunogenic peptide antigens especially self proteins for the treatment of diseases associated with expression of those antigens. If the PA is human PSM (undefined), (I) is used for the treatment of prostate **cancer**. If the PA is human fibroblast growth factor (FGF) 8b, (I) is used for the treatment of prostate **cancer** or breast **cancer**. If the PA is Her2, (I) is used for the treatment of breast **cancer** (claimed).

Dwg.0/6

L10 ANSWER 4 OF 38 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3

ACCESSION NUMBER: 2000:534597 BIOSIS

DOCUMENT NUMBER: PREV200000534597

TITLE: A therapeutic human anti-idiotypic antibody mimics **CD55** in three distinct regions.

AUTHOR(S): Spendlove, Ian (1); Li, Li; Potter, Vanessa; Christiansen, Dale; Loveland, Bruce E.; Durrant, Lindy G.

CORPORATE SOURCE: (1) CRC Academic Unit of Clinical Oncology, University of Nottingham, City Hospital, Hucknall Rd, Nottingham, NG5 1PB UK

SOURCE: European Journal of Immunology, (October, 2000) Vol. 30, No. 10, pp. 2944-2953. print.
ISSN: 0014-2980.

DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The human anti-idiotypic antibody 105AD7 was isolated from a colorectal **cancer** patient receiving the anti-**tumor** antibody **791T**/36 for radioimmuno-scintigraphy of liver metastases. We have mapped the binding site of **791T**/36 to the first two small consensus repeat (SCR) domains of the complement regulatory **protein** (**CD55**) that is overexpressed by a wide range of solid **tumors**. Cloning of both **antigen** and anti-idiotype has identified the molecular basis of their mimicry. Amino acid homology has been identified between three complementarity-determining regions of 105AD7 and three regions of **CD55** within the first two SCR domains. **791T**/36 and anti-anti-idiotypic (Ab3) polyclonal antibodies raised against 105AD7 showed specific binding to these **peptides**. The antibodies were also found to bind synergistically to combinations of these **peptides**, indicating cooperativity between the **peptides** in stabilizing antibody binding. This also implies that the contact face on both **CD55 antigen** and 105AD7 is generated by the cooperation of several **peptides** positioned on two domains in each **protein**. Thus a human monoclonal anti-idiotypic antibody generated by a **cancer** patient is able to show both amino acid and structural homology with the complement regulatory **protein CD55**. These findings help identify the mechanism by which a human anti-idiotypic antibody is able to mimic a **tumor**-associated **antigen** and stimulate anti-**tumor** B and T cell responses.

L10 ANSWER 5 OF 38 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:216993 BIOSIS
DOCUMENT NUMBER: PREV200000216993
TITLE: DNA **vaccine** for colorectal **cancer**
AUTHOR(S): Durrant, Lindy G. (1); Spendlove, Ian (1); Potter, Vanessa (1)
CORPORATE SOURCE: (1) Univ of Nottingham, Nottingham UK
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 470.
Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA April 01-05, 2000
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

SUMMARY LANGUAGE: English

L10 ANSWER 6 OF 38 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000155109 MEDLINE
DOCUMENT NUMBER: 20155109 PubMed ID: 10690519
TITLE: A neoadjuvant clinical trial in colorectal **cancer** patients of the human anti-idiotypic antibody 105AD7, which mimics **CD55**.
AUTHOR: Durrant L G; Maxwell-Armstrong C; Buckley D; Amin S; Robins R A; Carmichael J; Scholefield J H
CORPORATE SOURCE: Cancer Research Campaign Academic Unit of Clinical Oncology, University of Nottingham, United Kingdom.. Lindy.durrant@nott.ac.uk
SOURCE: CLINICAL CANCER RESEARCH, (2000 Feb) 6 (2) 422-30. Journal code: C2H; 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000328

AB Thirty-five patients received 105AD7 human anti-idiotype **vaccination** prior to surgery for colorectal **carcinoma**. Patients were **immunized** before and also received one to two **immunizations** after surgical resection of their colorectal **cancer**. The **vaccine** was well tolerated with no associated toxicity. Lymphocytic infiltration within the resected **tumors** was quantified by immunohistochemistry and image analysis. Enhanced infiltration of helper T cells (CD4) and natural killer (NK) cells (CD56) were observed in the **tumors** from **immunized** patients when compared with **tumors** from stage, grade, site, age, and sex matched unimmunized patients. NK activity was increased in the blood, peaking 7-10 days post **immunization** and then dropping rapidly and correlating with NK extravasation within the **tumor**. Comparison of the amino acid sequences of 105AD7 anti-idiotype and the antigen it mimics, **CD55**, has predicted that patients with HLA-DR1, HLA-DR3, and HLA-DR7 haplotypes should show helper T cell responses following 105AD7 **vaccination**. Eighty-three percent of patients expressing these haplotypes responded to 105AD7, whereas 88% of patients who failed to express these haplotypes were nonresponders. With a median follow-up of 4 years (range, 2.5-6 years) 65% of patients remained disease free. This trial shows that 105AD7 stimulates

antitumor inflammatory responses allowing extravasation within **tumor** deposits of both helper T cells and NK cells. This represents a way of evaluating immune responses in patients both within the blood and at the **tumor** site. The study confirms that **immunization** with a human anti-idiotypic antibody results in immune responses in 83% of patients with a permissive haplotype.

L10 ANSWER 7 OF 38 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2000054382 MEDLINE
DOCUMENT NUMBER: 20054382 PubMed ID: 10585589
TITLE: 105Ad7 **cancer vaccine** stimulates anti-**tumour** helper and cytotoxic T-cell responses in colorectal **cancer** patients but repeated **immunisations** are required to maintain these responses.
AUTHOR: Durrant L G; Buckley D J; Robins R A; Spendlove I
CORPORATE SOURCE: CRC Department of Clinical Oncology, University of Nottingham, Nottingham, UK.. lindy.durrant@nott.ac.uk
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (2000 Jan 1) 85 (1) 87-92.
Journal code: GQU; 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000106

AB 105AD7 is a human anti-idiotypic antibody that recognises the binding site of the anti-**tumour** antibody **791T**/36 and can thereby mimic the **CD55 antigen**. The molecular basis of 105AD7 mimicry has been identified with 3 CDR regions of 105AD7 showing similarity to 3 regions of **CD55**. These regions have been analysed for potential T-cell epitopes, and sequences that are predicted to bind to HLA/A1, 3,24 and to HLA/DR1,3,7 have been identified within the CDRH3 region of 105AD7. These epitopes should be stimulating CD8 and CD4 responses, respectively. This prediction was tested on 12 colorectal **cancer** patients receiving 105AD7 therapy. There was good concordance in 10 of 11 patients between accumulation of CD8RO cells or **tumour** killing and expression of HLA/A1,3,24. The only patient who failed to respond had a non-permissive class II haplotype and failed to show a helper response. Again 10 of 11 patients showing accumulation of CD4RO cells, in vitro blastogenesis responses, enhanced IL-2 or enhanced NK activity expressed one or

more of the HLA/DR1,3,7 haplotypes. Although there was a consistent accumulation of CD45RO cells following 14 of 18 **immunisations**, only one patient showed a sustained memory response. Our results suggest that 105AD7 can stimulate CD4 and CD8 responses in patients with the appropriate haplotype. However, it may be necessary to continue to **immunise**, since few patients produce a sustained memory response.

L10 ANSWER 8 OF 38 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1999-540585 [45] WPIDS
DOC. NO. CPI: C1999-157880
TITLE: **Cancer vaccine** containing **CD 55** family **polypeptide** , to induce at least one of T helper, cytotoxic T cell or natural killer immune response.
DERWENT CLASS: B04 D16
INVENTOR(S): DURRANT, L G; SPENDLOVE, I
PATENT ASSIGNEE(S): (CANC-N) CANCER RES CAMPAIGN TECHNOLOGY
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9943800	A1	19990902	(199945)*	EN	83
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9926330	A	19990915	(200004)		
EP 1056851	A1	20001206	(200064)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9943800	A1	WO 1999-GB582	19990226
AU 9926330	A	AU 1999-26330	19990226
EP 1056851	A1	EP 1999-906367	19990226
		WO 1999-GB582	19990226

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 9926330 A Based on WO 9943800
EP 1056851 A1 Based on WO 9943800

PRIORITY APPLN. INFO: GB 1998-4065 19980226
AN 1999-540585 [45] WPIDS
AB WO 9943800 A UPAB: 19991103
NOVELTY - **Cancer vaccine** (A) comprises a **polypeptide** (I) of the **CD55** family, or its fragment or derivative, or a nucleic acid (II) that encodes (I).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) isolated and purified **791Tgp72 antigen** (Ag);
(2) composition containing Ag and a carrier; and
(3) method for isolating Ag from cells.
ACTIVITY - **Antitumor**.
MECHANISM OF ACTION - Induction of a specific immune response. **CD55** is overexpressed by **cancer** cells and serves to protect them against immune attack. If such cells fail to produce **CD55** they will be killed by complement- or natural killer-mediated lysis, but, in subjects **vaccinated** with (I), cells that do express (I) are also killed, by **CD55** -specific T cells.
USE - (A) induce at least one of T helper, cytotoxic T cell or natural killer immune responses, possibly also production of neutralizing antibodies and complement-mediated lysis, against (I), specifically the new **antigen 791Tgp72**, expressed by **cancer** cells. They are useful for treating **cancers**, e.g. colorectal, breast or ovarian **cancer** or osteosarcoma where these are associated with overexpression of **CD55**.
ADVANTAGE - (A) induce a response with greater affinity for **cancer** cells (which express (I) at high level) than non-**cancer** cells (which express (I) at lower levels).
Dwg.0/11

L10 ANSWER 9 OF 38 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:450246 SCISEARCH
THE GENUINE ARTICLE: 203NA
TITLE: Identification of a human anti-**CD55** single-chain Fv by subtractive panning of a phage library using **tumor** and **nontumor** cell lines
AUTHOR: Ridgway J B B; Ng E; Kern J A; Lee J; Brush J; Goddard A; Carter P (Reprint)
CORPORATE SOURCE: GENENTECH INC, DEPT MOL ONCOL, 1 DNA WAY, S SAN FRANCISCO, CA 94080 (Reprint); GENENTECH INC, DEPT

MOL ONCOL, S SAN FRANCISCO, CA 94080; GENENTECH INC, DEPT MOL BIOL, S SAN FRANCISCO, CA 94080; GENENTECH INC, DEPT PROT CHEM, S SAN FRANCISCO, CA 94080
COUNTRY OF AUTHOR: USA
SOURCE: CANCER RESEARCH, (1 JUN 1999) Vol. 59, No. 11, pp. 2718-2723.
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202.
ISSN: 0008-5472.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 52

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A large naive human single-chain (sc) Fv phage library was used to search for **tumor**-associated antigens by panning with a lung **adenocarcinoma** cell line, 1264, and counter-selecting with a **nontumor** bronchial epithelial cell line, BEAS-2B, After three rounds of subtractive panning, 239 of 673 clones analyzed bound selectively to 1264 **tumor** cells in a phage ELISA. Diversity analysis of these **tumor**-selective clones by BstNI fingerprinting and nucleotide sequencing revealed 14 distinct scFv fragments. Four clones bound selectively to 1264 over BEAS-2B cells when analyzed by a more discriminating flow cytometric assay using scFv, Moreover, these clones showed only Limited cross-reactivity to several primary human fell lines. One clone, LU30, also cross-reacted strongly with the lung **adenocarcinoma** line, A549, The LU30 antigen was identified as decay-accelerating factor (**CD55**) by expression cloning from a 1264 cDNA library. The mean number of decay-accelerating factor molecules on the surface of 1264 and BEAS cells used for panning and counter-selection was estimated as 75,000 +/- 5,000 and 13,000 +/- 10,000, respectively. Thus; phage library panning combined with-expression cloning permits identification of antibodies and their cognate antigens for **proteins** that are differentially expressed on the surface of distinct cell populations.

L10 ANSWER 10 OF 38 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1999274526 MEDLINE
DOCUMENT NUMBER: 99274526 PubMed ID: 10344729
TITLE: Decay accelerating factor (**CD55**): a target for **cancer vaccines**?.
AUTHOR: Spendlove I; Li L; Carmichael J; Durrant L G
CORPORATE SOURCE: Cancer Research Campaign Academic Unit of Clinical Oncology, University of Nottingham, City Hospital, United Kingdom.. Ian.Spendlove@Nottingham.ac.uk
SOURCE: CANCER RESEARCH, (1999 May 15) 59 (10) 2282-6.

Journal code: CNF; 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990628
Last Updated on STN: 19990628
Entered Medline: 19990617

AB The **791Tgp72 antigen** has been used successfully as a target for **tumor** imaging and T-cell immunotherapy. We have characterized this **antigen** using the monoclonal antibody **791T**/36 as a 72/66 kDa doublet. NH2-terminal **protein** sequencing of the two bands revealed identity with the complement regulatory **protein CD55**. Antibodies recognizing different domains of **CD55** were also shown to bind to the purified **791Tgp72**, although sequence analysis of the cDNA cloned from **791T tumor** cells showed 100% homology with **CD55** and transfection of the cDNA into **antigen**-negative CHO cells resulted in binding of **791T**/36. This identifies the **tumor antigen 791Tgp72** as **CD55**. This **protein** protects cells from complement attack; however, it can also transduce signals in lymphocytes and is a ligand for CD97, expressed by activated T cells. These results suggest that **CD55** plays a role in signaling between the innate and adaptive immune responses. It is therefore a very intriguing target, because absence of the molecule makes the **tumor** cells susceptible to complement, whereas protective overexpression results in the **antigen** being a target for T-cell immunotherapy.

L10 ANSWER 11 OF 38 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 1999417652 MEDLINE
DOCUMENT NUMBER: 99417652 PubMed ID: 10486371
TITLE: Increased activation of lymphocytes infiltrating primary colorectal **cancers** following **immunisation** with the anti-idiotypic monoclonal antibody 105AD7.
AUTHOR: Maxwell-Armstrong C A; Durrant L G; Robins R A; Galvin A M; Scholefield J H; Hardcastle J D
CORPORATE SOURCE: University Department of Surgery, Queen's Medical Centre, Nottingham NG7 2UH, UK.
SOURCE: GUT, (1999 Oct) 45 (4) 593-8.
Journal code: FVT; 2985108R. ISSN: 0017-5749.
PUB. COUNTRY: ENGLAND: United Kingdom
(CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CLINICAL TRIAL, PHASE II)

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991101

AB BACKGROUND: The anti-idiotypic monoclonal antibody 105AD7 mimics the **tumour** associated **antigen 791Tgp72**, expressed on 70-80% of colorectal **cancers**. Phase I studies have shown that the **vaccine** is non-toxic, and a number of patients have been **immunised** prior to resection of their primary **tumours**. AIMS: To assess lymphocyte activation at the **tumour** site by measuring expression of the alpha subunit of the interleukin 2 receptor (CD25). METHODS: Nineteen patients with primary colorectal **cancer** were **immunised** with varying doses of 105AD7 prior to resection of their primary **tumours**. Samples of normal bowel and **tumour** edge/centre from 16 patients were available for immunohistochemical staining with a monoclonal antibody against CD25. Samples from a matched control group were also stained. Fresh **tumours** from 14 **immunised** patients and 31 unimmunised control patients were disaggregated, and the lymphocytes obtained labelled for CD25. Samples were analysed blindly by flow cytometry. RESULTS: Median infiltration of lymphocytes expressing CD25, measured immunohistochemically, was higher in trial patients, as was the ratio of **tumour** to normal bowel infiltration. Flow cytometric analysis of fresh **tumour** from **immunised** patients showed a significantly higher percentage of lymphocytes expressing CD25 **tumour** infiltrating lymphocytes than their matched and unmatched controls. DISCUSSION: The alpha subunit of the interleukin 2 receptor is increased on **tumour** infiltrating lymphocytes, in patients **immunised** with the colorectal **cancer** **vaccine** 105AD7. This suggests a population of activated lymphocytes capable of targeting **791Tgp72** expressing **tumour** cells, such as circulating micrometastases. 105AD7 may have a role as adjuvant therapy in early stage disease.

L10 ANSWER 12 OF 38 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 1999334867 MEDLINE
DOCUMENT NUMBER: 99334867 PubMed ID: 10408382
TITLE: Neutralization of complement regulatory proteins augments lysis of breast **carcinoma** cells targeted with rhumAb anti-HER2.
AUTHOR: Jurianz K; Maslak S; Garcia-Schuler H; Fishelson Z; Kirschfink M
CORPORATE SOURCE: Institute of Immunology, University of Heidelberg,

Germany.
SOURCE: IMMUNOPHARMACOLOGY, (1999 May) 42 (1-3) 209-18.
Journal code: GY3; 7902474. ISSN: 0162-3109.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 19990925
Last Updated on STN: 20000303
Entered Medline: 19990915

AB The capacity of recombinant human monoclonal anti-p185HER2 IgG (rhumAb anti-HER2) to activate human complement was investigated. Complement activation by rhumAb anti-HER2 on various human breast **carcinoma** cell lines resulted in deposition of complement **proteins** on these cells. Complement activation was also observed in a solid-phase binding assay, in which purified p185HER2 was immobilized onto a microtiter plate. rhumAb anti-HER2 induced some complement-mediated **tumor** cell lysis by rabbit complement, but not by human complement. Analysis of membrane complement regulatory **proteins** (mCRP) on breast **carcinoma** cells revealed a heterogenous expression of CD46, **CD55** and CD59. After blocking the mCRP activity with specific antibodies, rhumAb anti-HER2 induced about 15% lysis of p185HER2-expressing **tumor** cells. **Tumor** cell sensitization with rabbit polyclonal anti-**tumor** antiserum following mCRP neutralization, augmented cell lysis from 10 to 80%. Expression of mCRP was upregulated by treatment with PMA, and correlated with increased protection of the **tumor** cells from complement lysis. These results suggest that humanized antibodies like rhumAb anti-HER2 promote complement activation leading to **tumor** cell phagocytosis and cell-mediated cytotoxicity. They further demonstrate that a successful **tumor** immunotherapeutical approach, based on antibody and complement treatment, requires mCRP neutralization.

L10 ANSWER 13 OF 38 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 1998162428 MEDLINE
DOCUMENT NUMBER: 98162428 PubMed ID: 9501807
TITLE: Colorectal **cancer vaccines**.
AUTHOR: Maxwell-Armstrong C A; Durrant L G; Scholefield J H
CORPORATE SOURCE: Department of Surgery, University of Nottingham, UK.
SOURCE: BRITISH JOURNAL OF SURGERY, (1998 Feb) 85 (2) 149-54.
Ref: 65
Journal code: B34; 0372553. ISSN: 0007-1323.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980407
Last Updated on STN: 19980407
Entered Medline: 19980326

AB BACKGROUND: Advances in molecular pathology have enabled a number of colorectal **cancer antigens** to be identified and characterized. The commonest investigated include 17-1A, **791Tgp72** and **carcinoembryonic antigen**. **Vaccines** have been developed that stimulate the immune system to target these **antigens**. This paper reviews current areas of research in this field. METHODS AND RESULTS: Relevant articles were obtained on **vaccines** for colorectal **cancer** from Medline and the Bath Information Data System. A number of approaches are currently being evaluated in Phase I, II and III trials. These include anti-idiotypic antibody **immunization**, DNA **vaccines**, mucin and heat shock protein-based **vaccines**, oncogenes and viral vectors. CONCLUSION: Evidence is accumulating to suggest that immune responses may be generated against colorectal **cancer** using these approaches. While the concept of **vaccination** against this malignancy is essentially experimental, surgeons should be aware of current advances.

L10 ANSWER 14 OF 38 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:112650 BIOSIS
DOCUMENT NUMBER: PREV199900112650
TITLE: DNA encoding the scFv of the human anti-idiotypic antibody 105AD7 - studies comparing mono-, di- and trimeric constructs.
AUTHOR(S): Potter, V.; Spendlove, I.; Durrant, L. G.
CORPORATE SOURCE: CRC Dep. Clin. Oncol., City Hosp., Nottingham NG5 1PB UK
SOURCE: Immunology, (Dec., 1998) Vol. 95, No. SUPPL. 1, pp. 32.
Meeting Info.: 6th Annual Congress of the British Society for Immunology Harrogate, England, UK December 1-4, 1998
ISSN: 0019-2805.
DOCUMENT TYPE: Conference
LANGUAGE: English

L10 ANSWER 15 OF 38 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 1998057323 MEDLINE
DOCUMENT NUMBER: 98057323 PubMed ID: 9396616
TITLE: **Cancer vaccines**.

AUTHOR: Durrant L G
CORPORATE SOURCE: CRC Department of Clinical Oncology, University of Nottingham, City Hospital, UK.
SOURCE: ANTI-CANCER DRUGS, (1997 Sep) 8 (8) 727-33. Ref: 39
Journal code: A9F; 9100823. ISSN: 0959-4973.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980130
Last Updated on STN: 19980130
Entered Medline: 19980116

AB A better understanding of immune recognition of cells has led to identification of potential new targets on **tumor** cells. Noticeable successes in melanoma have been **immunization** with the GM2 ganglioside **vaccine**, and the identification of novel **antigens** such as MAGE, BAGE and GAGE recognized by T cells cloned from **cancer** patients with regressing disease. However, the unexpected finding that other **antigens** recognized by these T cells were overexpressed normal differentiation **antigens** such as tyrosinase. Pmel 17 and Melan A have led to **vaccines** developed against differentiation **antigens** expressed in other solid **tumors**. Monoclonal antibody, anti-idiotype and **antigen** based **vaccines** for colorectal target **antigens** 17-1A, CEA and **791Tgp72** are all in clinical development. Similarly HER2/neu and mucin overexpression in breast **cancer** represent promising targets. Mutations in **tumor** oncogenes or suppressor genes which lead to malignant transformation can also present **tumor**-specific **antigens**. The most effective **vaccines** against infectious disease are live viruses. The development of DNA **vaccines** which act like viruses in entering cells and show continuous production of **antigens** offers great potential for the future.

L10 ANSWER 16 OF 38 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 97239462 MEDLINE
DOCUMENT NUMBER: 97239462 PubMed ID: 9085124
TITLE: Low doses of 105AD7 **cancer vaccine** preferentially stimulate anti-**tumor** T-cell immunity.
AUTHOR: Durrant L G; Buckley D J; Spendlove I; Robins R A
CORPORATE SOURCE: CRC Department of Clinical Oncology, Nottingham University, UK.

SOURCE: HYBRIDOMA, (1997 Feb) 16 (1) 23-6.
Journal code: GFS; 8202424. ISSN: 0272-457X.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CLINICAL TRIAL, PHASE II)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970908
Last Updated on STN: 20000303
Entered Medline: 19970827

AB Clinical studies with the human anti-idiotypic antibody 105AD7 have clearly shown that **791Tgp72** is a good target **antigen** for cell-mediated immunity. No antibody-related toxicity was observed in any of the 135 patients entered into phase I/II clinical trials of 105AD7, whereas both helper and cytotoxic T-cell responses were induced. The helper responses were exemplified by induction of interleukin-2 (IL-2), **antigen**-specific blastogenesis, and enhanced natural killer (NK) activity. Anti-**tumor** cytotoxicity was measured directly and was supported by activation of circulating CD8 cells. In this study, it is shown that a 100-microgram injection of 105AD7 was more effective than the 200-microgram dose. Enhanced IL-2 production was observed following 15/19 injections of 100 micrograms of 105AD7 whereas only 4/11 injections of 200 micrograms of 105AD7 induced responses ($p < 0.02$). Similarly, time to progression was significantly ($p < 0.05$) slower (median 6 m) in patients injected with 100 micrograms than patients receiving the higher dose, suggesting that 100 micrograms or lower may be the optimal dose. The standard dose for hepatitis **vaccination** is 10 micrograms. In vitro blastogenesis assays on naive donors have shown that a dose of 105AD7, which is either too high or too low, fails to activate T cells. The optimal dose in vitro is 10 ng.

L10 ANSWER 17 OF 38 CANCERLIT
ACCESSION NUMBER: 96602215 CANCERLIT
DOCUMENT NUMBER: 96602215
TITLE: Clinical evidence that 105AD7, anti-idiotypic antibody, delays **tumor** growth by presenting a multiplex of T-cell epitopes which result in **antitumor** inflammatory responses (Meeting abstract).
AUTHOR: Durrant L G; Buckley T J; Robins R K
CORPORATE SOURCE: Department of Surgery, Nottingham University, NG7 2UH, UK.

SOURCE: Proc Annu Meet Am Assoc Cancer Res, (1995). Vol. 36, pp. A2920.
ISSN: 0197-016X.
DOCUMENT TYPE: (MEETING ABSTRACTS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199604

AB A human monoclonal anti-idiotypic antibody, 105AD7, which mimics a colorectal **tumor**-associated **antigen**, **791Tgp72**, has been developed. A Phase I trial in advanced colorectal **cancer** patients (pts) showed that 105AD7 was non toxic and that **immunized** pts had increased survival when compared with a contemporary group of pts treated in the same center. These encouraging results are currently being confirmed in a double blind randomized study in a similar cohort of pts. There is accumulating clinical evidence that 105AD7 delays **tumor** growth by presenting a multiplex of T-cell epitopes. Stimulation of helper T cells was exemplified in the phase I study as 105AD7 **immunized** pts showed **antigen** specific T-cell blastogenesis responses and enhanced IL-2 production. Further evidence was obtained from the new clinical study in which colorectal **cancer** pts were **immunized** prior to **tumor** resection. Immune infiltrating cells were analyzed by immunohistochemistry and effector cell function was studied in immune cells from peripheral blood and **tumor** draining lymph nodes. Both activated CD4 and natural killer (NK) cells were observed at the **tumor** site, which is of interest as NK cells are rarely found in colorectal **tumors**. Effector studies confirmed that NK activity was enhanced in 3/6 pts. Increased autologous **tumor** killing was also found in 3/4 pts and accumulation of CD8RO cells following 105AD7 **immunization** also suggested that CD8 T cells were being stimulated.

L10 ANSWER 18 OF 38 MEDLINE DUPLICATE 12

ACCESSION NUMBER: 96084042 MEDLINE
DOCUMENT NUMBER: 96084042 PubMed ID: 7492753
TITLE: Clinical evidence that the human monoclonal anti-idiotypic antibody 105AD7, delays **tumor** growth by stimulating anti-**tumor** T-cell responses.
AUTHOR: Buckley D T; Robins A R; Durrant L G
CORPORATE SOURCE: Department of Surgery, Nottingham University, UK.
SOURCE: HUMAN ANTIBODIES AND HYBRIDOMAS, (1995) 6 (2) 68-72.
Journal code: A6A; 9014461. ISSN: 0956-960X.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960217
Last Updated on STN: 19960217
Entered Medline: 19960111

AB A human monoclonal anti-idiotypic antibody, 105AD7, which mimics a colorectal **tumor** associated **antigen**, **791Tgp72**, has been developed. A Phase I trial in advanced colorectal **cancer** patients showed that 105AD7 therapy was nontoxic and that **immunised** patients had prolonged survival when compared to a contemporary group of patients treated in the same center. There is accumulating clinical evidence that 105AD7 delays **tumor** growth by stimulating anti-**tumor** T-cell responses. Stimulation of helper T-cells was exemplified in the phase I study as 105AD7 **immunized** patients showed **antigen** specific T-cell blastogenesis responses and enhanced IL-2 production. Further evidence was obtained from a new clinical study in which colorectal **cancer** patients were **immunized** prior to **tumor** resection. Immune infiltrating cells were analysed by immunohistochemistry and effector cell function was studied in immune cells from peripheral blood and **tumor** draining lymph nodes. Both activated CD4 and natural killer (NK) cells were observed at the **tumor** site, which is of interest as NK cells are rarely found in colorectal **tumors**. Effector studies confirmed that NK activity was enhanced in 3/6 patients. Increased autologous **tumor** killing was also found in 3/4 patients and accumulation of CD8RO cells following 105AD7 **immunization** also suggested that CD8 T cells were being stimulated.

L10 ANSWER 19 OF 38 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 95221031 MEDLINE
DOCUMENT NUMBER: 95221031 PubMed ID: 7705934
TITLE: Induction of cellular immune responses by a murine monoclonal anti-idiotypic antibody recognizing the **791Tgp72 antigen** expressed on colorectal, gastric and ovarian human **tumours**.
AUTHOR: Durrant L G; Doran M; Austin E B; Robins R A
CORPORATE SOURCE: Department of Surgery, University of Nottingham, UK.
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (1995 Mar 29) 61 (1) 62-6.
Journal code: GQU; 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

Searcher : Shears 308-4994

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950518
Last Updated on STN: 19950518
Entered Medline: 19950509

AB There is accumulating evidence that cellular rather than antibody responses are more effective for **tumour** rejection. It is therefore important to screen anti-idiotypic (anti-id) antibodies for their ability to stimulate anti-**tumour** T-cell responses. The human anti-id monoclonal antibody (MAb) 105AD7 stimulated both delayed-type hypersensitivity (DTH) responses in animals and **antigen**-specific blastogenesis and IL-2 induction in advanced **cancer** patients. It may not be necessary to use human anti-id antibodies as murine anti-id antibodies, which elicit DTH responses against immunodominant human T-cell epitopes and may be just as useful in the clinic. We have therefore produced a murine anti-id antibody to the same MAb as was used to generate the human anti-id antibody and screened it for its ability to generate cellular anti-**tumour** immune responses. Low-dose **immunization** with the murine anti-id MAb NCRC60, which recognises the paratope of the anti-**791Tgp72** MAb **791T**/36, induced DTH responses to **791Tgp72** -expressing **tumour** cells but not to **antigen** -negative cells. DTH responses with no detectable antibody responses were induced with 5 micrograms of anti-id NCRC60 without adjuvant. Addition of either complete Freund's adjuvant or Quil A did not enhance DTH responses. However, when the anti-id NCRC60 was linked to KLH and injected in the presence of Freund's adjuvant anti-anti-id antibodies and anti-**791Tgp72** antibodies were induced. NCRC60 anti-id was also capable in vitro of priming human T cells from **cancer** patients to proliferate in response to secondary stimulation with **791Tgp72**-expressing **tumour** cells, suggesting that it may have therapeutic potential in **cancer** patients.

L10 ANSWER 20 OF 38 CANCERLIT
ACCESSION NUMBER: 96646811 CANCERLIT
DOCUMENT NUMBER: 96646811
TITLE: Clinical evidence that the human monoclonal anti-idiotypic antibody 105AD7 delays **tumor** growth by stimulating anti-**tumor** T-cell responses (Meeting abstract).
AUTHOR: Durrant L G; Buckley T J; Robins R A
CORPORATE SOURCE: Depts of Surgery and Immunology, Univ. Hospital, Nottingham University, Nottingham, NG7 2UH, UK.
SOURCE: Hum Antibodies Hybridomas, (1995). Vol. 6, No. 1. ISSN: 0956-860X.
DOCUMENT TYPE: (MEETING ABSTRACTS)

FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199607
AB A human monoclonal anti-idiotypic antibody (105AD7), which mimics a colorectal **tumor**-associated **antigen** (**791Tgp72**) has been developed. A Phase I trial in advanced colorectal **cancer** patients showed that 105AD7 was non-toxic and that **immunized** patients had increased survival when compared with a contemporary group of patients treated in the same centre. These encouraging results are currently being confirmed in a double blind randomized study in a similar cohort of patients. There is accumulating clinical evidence that 105AD7 delays **tumor** growth by stimulating anti-**tumor** T-cell responses. Stimulation of helper T-cells was exemplified in the Phase I study as 105AD7 **immunized** patients showed **antigen** specific T-cell blastogenesis responses and enhanced IL-2 production. Further evidence was obtained from the new clinical study in which colorectal **cancer** patients were **immunized** prior to **tumor** resection. Immune infiltrating cells were analyzed by immunohistochemistry and effector cell function was studied in immune cells from peripheral blood and **tumor**-draining lymph nodes. Both activated CD4 and natural killer (NK) cells were observed at the **tumor** site, which is of interest as NK cells are rarely found in colorectal **tumors**. Effector studies confirmed that NK activity was enhanced in 3/6 patients. Increased autologous **tumor** killing was also found in 3/4 patients and accumulation of CD8RO cells following 105AD7 **immunization** also suggested that CD8 T-cells were being stimulated.

L10 ANSWER 21 OF 38 CANCERLIT
ACCESSION NUMBER: 96605289 CANCERLIT
DOCUMENT NUMBER: 96605289
TITLE: Antigen processing is essential for induction of **antitumor** immunity by 105AD7 **vaccine** (Meeting abstract).
AUTHOR: Buckley D T; Robins R A; Durrant L G
CORPORATE SOURCE: Dept. of Surgery, Univ. of Nottingham, UK.
SOURCE: Br J Cancer, (1994). Vol. 71, Suppl. 24, pp. 11. ISSN: 0007-0920.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199605
AB The human monoclonal antibody 105AD7 stimulates cellular **antitumor** immune responses in **cancer** patients. These can be monitored by in vitro proliferative responses to challenge with 105AD7 but not human IgG1 or to challenge with

791Tgp72 positive but not negative **tumor** cells. However, due to the limitation on the amount of blood that can be ethically taken from **cancer** patients, an assay was developed to detect blastogenesis responses to 105AD7 in healthy nonimmunized donors. This allows repeated analysis of responses to 105AD7 in the same donor which is essential for studying the mechanism of processing and presentation of 105AD7 in the induction of **antitumor** immune responses. Briefly lymphocytes from donors are stimulated in bulk (2 x 10(6) cells in a well of a 24 well plate) with a range of doses of 105AD7 for 3 days, the cultures are then fed with 10% FCS and IL-2 (10 units/ml) and then cells are harvested and pulsed with thymidine daily between days 5-10. **Antigen** presenting cells are either present throughout the assay or they are processed separately by exposing peptide to peripheral blood mononuclear cells (PBMC) for several hours, washing and irradiating the cells prior to exposing to the responder cells. Responder cells are either unfractionated PBMC or nylon wool purified T-cells. Two donors who consistently respond to 105AD7 stimulation have been identified. Dose response curves have suggested that the optimal dose of 105AD7 is 1 ng/ml for both donors and detectable blastogenesis responses to this dose can be observed 8-9 days in culture. Responses in **immunized** patients can be detected at 5 days which probably reflects their higher precursor frequency. Experiments on 105AD7 processing have suggested that **antigen** presenting cells are essential and that 105AD7 must be present for several days to induce T-cell proliferation. In contrast the same donor lymphocytes pulsed with a tetanus toxoid T-cell peptide for 2 hours respond with a brisk proliferation 6-8 days later. These results indicate that 105AD7 requires processing prior to induction of immune responses.

L10 ANSWER 22 OF 38 CANCERLIT
ACCESSION NUMBER: 96605257 CANCERLIT
DOCUMENT NUMBER: 96605257
TITLE: 105AD7 anti-idiotype antibodies in colorectal **cancer** (Meeting abstract).
AUTHOR: Durrant L G
CORPORATE SOURCE: Dept. of Clinical Oncology, Cancer Research Campaign, Univ. of Nottingham NG5 1PB, UK.
SOURCE: Br J Cancer, (1994). Vol. 71, Suppl. 24, pp. 1. ISSN: 0007-0920.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199605
AB A human monoclonal anti-idiotypic antibody, 105AD7 (Austin et al, Immunology 67:525, 1989), a murine anti-idiotypic antibody NCRC60 and the human polyclonal response to **791T**/36 all recognize

a similar dominant binding site on the **791T**/36 and mimic the target **antigen 791Tgp72**. Expression of this **antigen** on colorectal **tumors** is associated with a bad prognosis which is unrelated to **tumor** stage or differentiation. Both the murine and the human monoclonal antibodies evoke T-cell responses to **791Tgp72 antigen** on human **tumor** cells (Austin et al, J Natl **Cancer** Inst 83:1245, 1991) and thus identify a new target for active specific immunotherapy. A phase I trial in advanced colorectal **cancer** patients showed that the human monoclonal antibody 105AD7 was nontoxic and that **immunized** patients had delayed **tumor** growth and increased survival when compared with a contemporary group of patients treated in the same center (Denton et al, Int J **Cancer** 57:10, 1994). These encouraging results are currently being confirmed in a double-blind randomized study in a similar cohort of patients. There is accumulating clinical evidence that 105AD7 delays **tumor** growth by stimulating both helper and cytotoxic immune responses. Stimulation of helper T-cells was exemplified in the phase I study as 105AD7 **immunized** patients showed **antigen** specific T-cell blastogenesis responses and enhanced IL-2 production (Robins et al, **Cancer** Res 51:5425, 1991). Further evidence was obtained from the new clinical study in which colorectal **cancer** patients were **immunized** prior to **tumor** resection. Immune infiltrating cells were analyzed by immunohistochemistry and effector cell function was studied in immune cells from peripheral blood and **tumor** draining lymph nodes. Both activated CD4 and natural killer (NK) cells were observed at the **tumor** site, which is of interest as NK cells are rarely found in colorectal **tumors**. Effector studies confirmed that NK activity was enhanced in 3/6 patients (Durrant et al, **Cancer** Res 54:4837, 1994). Increased autologous **tumor** killing was also found in 3/4 patients and accumulation of CD8RO cells following 105AD7 **immunization** also suggested that CD8 T-cells were being stimulated.

L10 ANSWER 23 OF 38 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 92005468 MEDLINE
DOCUMENT NUMBER: 92005468 PubMed ID: 1913661
TITLE: **Antitumor** immune response and interleukin 2 production induced in colorectal **cancer** patients by **immunization** with human monoclonal anti-idiotypic antibody.
AUTHOR: Robins R A; Denton G W; Hardcastle J D; Austin E B; Baldwin R W; Durrant L G
CORPORATE SOURCE: Cancer Research Campaign Laboratories, University of Nottingham, United Kingdom.

Searcher : Shears 308-4994

SOURCE: CANCER RESEARCH, (1991 Oct 1) 51 (19) 5425-9.
Journal code: CNF; 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19970203
Entered Medline: 19911029

AB The immunogenicity of human anti-idiotypic antibody has been investigated using a human monoclonal anti-idiotypic antibody (105AD7) which interacts with the binding site of **791T**/36, a mouse monoclonal antibody against gp72 **antigen**. This **antigen** is frequently expressed in gastrointestinal **cancer**, therefore, six patients with advanced colorectal **cancer** have been **immunized** with 105AD7 as an aluminum hydroxide gel precipitate in a phase I clinical study. Cryopreserved blood mononuclear cells were tested for in vitro proliferative responses by [3H]thymidine incorporation; plasma samples were tested by enzyme-linked immunosorbent assay for anti-anti-idiotypic and **antitumor** antibodies, and for interleukin 2. Proliferative responses to gp72 positive **tumor** cells were seen in four of five patients tested; parallel in vitro responses to 105AD7 anti-idiotypic antibody were seen in most of these patients. Interleukin 2 was detected in the plasma of four of six patients after 105AD7 **immunization**, with peak levels up to 7 units/ml. No toxicity related to anti-idiotype **immunization** and no **antitumor** or anti-anti-idiotype antibodies were seen. This study shows that human monoclonal anti-idiotype 105AD7 is immunogenic in **cancer** patients, inducing cellular **antitumor** responses and interleukin 2 production. This suggests that human monoclonal anti-idiotype antibodies may have considerable potential for immunotherapy of human **cancer**.

L10 ANSWER 24 OF 38 CANCERLIT

ACCESSION NUMBER: 92679897 CANCERLIT
DOCUMENT NUMBER: 92679897
TITLE: HUMAN MONOCLONAL ANTIBODIES.
AUTHOR: Austin E B
CORPORATE SOURCE: Univ. of Nottingham, UK.
SOURCE: Diss Abstr Int [B], (1991). Vol. 52, No. 4, pp. 1939.
ISSN: 0419-4217.
DOCUMENT TYPE: (THESIS)
FILE SEGMENT: ICDB
LANGUAGE: English

ENTRY MONTH: 199203

AB The isolation of human monoclonal antibodies with potential for therapy of **cancer** was investigated. Two types of antibodies were sought, (1) those recognizing **tumor antigens** and (2) anti-idiotypic antibodies capable of inducing autologous **antitumor** responses. Lymphocytes were fused with either the mouse myeloma P3NS1 or one of the alternative heteromyeloma fusion partners F10E5 or EL41 developed in this study. In a series of 44 fusions numerous hybridomas secreting **antigen** reactive immunoglobulin were produced. However, few hybridomas remained stable; one from a P3NS1 fusion and 3 from EL41. Three IgM antibodies reactive with autologous **tumor** were characterized. These antibodies stained colorectal **tumor** cells on frozen sections with weaker reactivity against surrounding 'normal' mucosa. Cell surface staining of primary freshly disaggregated colorectal **tumor** cells was observed. Two of the antibodies also reacted with the cell surface of T and B lymphocytes. However, fixed cytospin preparations of **tumor** cell lines showed the antibodies reacted with intracellular **antigens**, and cross-reacted with auto-**antigens** such as DNA. It is concluded that these antibodies were not generated in response to **tumor** and may have limited use for **tumor** therapy. For the alternative approach to **tumor** therapy, ie, that of idiotypic manipulation, a human IgG1 anti-idiotypic antibody 105AD7 was produced. This antibody was derived following fusion of EL41 with lymphocytes from a patient with colorectal **cancer** who had received the mouse **antitumor** antibody **791T/36** for **tumor** immunoscintigraphy. Characterization of 105AD7 demonstrated that it specifically bound to the **antigen** binding region of **791T/36**. **Immunization** of animals with 105AD7 produced both cellular and humoral **antitumor** responses indicating that this antibody may have a potential role in the therapy of human **cancer**. Based on the above, a Phase I clinical trial in advanced colorectal **cancer** patients has been initiated. (Available from UMI in association with The British Library. Requires signed TDF. Full text available from University Microfilms International, Ann Arbor, MI, as Order No. AADD--92951).

L10 ANSWER 25 OF 38 MEDLINE DUPLICATE 15

ACCESSION NUMBER: 91332941 MEDLINE

DOCUMENT NUMBER: 91332941 PubMed ID: 1870151

TITLE: Induction of delayed hypersensitivity to human **tumor** cells with a human monoclonal anti-idiotypic antibody.

AUTHOR: Austin E B; Robins R A; Baldwin R W; Durrant L G

CORPORATE SOURCE: Cancer Research Campaign Laboratories, Nottingham University, U.K.

SOURCE: JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1991 Sep 4) 83 (17) 1245-8.
Journal code: J9J; 7503089. ISSN: 0027-8874.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199109
ENTRY DATE: Entered STN: 19911006
Last Updated on STN: 19970203
Entered Medline: 19910918

AB There is considerable interest in the development of anti-idiotypic antibodies as **vaccines** in a number of diseases, including **cancer**. We have developed a human anti-idiotypic monoclonal antibody (105AD7) which binds at or very near to the binding site of mouse **antitumor** monoclonal antibody **791T**/36. The **791T**/36 antibody binds to a **tumor**-associated **antigen** (gp72) expressed on a number of human **tumors**, including colorectal and ovarian **carcinomas** and osteogenic sarcoma. This study shows that, in rats and mice, 105AD7 induces delayed-type hypersensitivity to human **tumor** cells bearing the gp72 **antigen**. Local transfer of delayed hypersensitivity was also demonstrated using lymphocytes from mice primed with 105AD7. These findings show that the human monoclonal anti-idiotypic antibody 105AD7 is likely to induce cellular immune responses to **tumors** in **cancer** patients.

L10 ANSWER 26 OF 38 MEDLINE DUPLICATE 16
ACCESSION NUMBER: 90380464 MEDLINE
DOCUMENT NUMBER: 90380464 PubMed ID: 2144742
TITLE: Syngeneic anti-idiotypic antibody prevents localization of a murine monoclonal antibody in human **tumour** xenografts.
AUTHOR: Pimm M V; Baldwin R W
CORPORATE SOURCE: Cancer Research Campaign Laboratories, University of Nottingham, U.K.
SOURCE: EUROPEAN JOURNAL OF CANCER, (1990) 26 (5) 567-8.
Journal code: ARV; 9005373. ISSN: 0959-8049.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199010
ENTRY DATE: Entered STN: 19901122
Last Updated on STN: 19901122
Entered Medline: 19901024

AB BALB/c mice were **immunized** against syngeneic mouse monoclonal antibody (Mab) **791T**/36 to produce

anti-idiotypic antibody. To examine the effect of this antibody on **tumour** localization of the Mab, serum from these mice was transferred to nude mice with human **tumour** xenografts and distribution was studied with I-125 labelled Mab. Serum containing anti-idiotypic antibody prevented **tumour** localization of the Mab. This finding has implications for the clinical use of human or humanized Mab since, if these evoke anti-idiotypic antibody, this alone may be sufficient to prevent **tumour** targeting.

L10 ANSWER 27 OF 38 MEDLINE DUPLICATE 17
ACCESSION NUMBER: 90234635 MEDLINE
DOCUMENT NUMBER: 90234635 PubMed ID: 2331436
TITLE: A bispecific monoclonal antibody against methotrexate and a human **tumour** associated antigen augments cytotoxicity of methotrexate-carrier conjugate.
AUTHOR: Pimm M V; Robins R A; Embleton M J; Jacobs E; Markham A J; Charleston A; Baldwin R W
CORPORATE SOURCE: Cancer Research Campaign Laboratories, University of Nottingham, UK.
SOURCE: BRITISH JOURNAL OF CANCER, (1990 Apr) 61 (4) 508-13. Journal code: AV4; 0370635. ISSN: 0007-0920.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
ENTRY DATE: Entered STN: 19900706
Last Updated on STN: 19970203
Entered Medline: 19900607

AB A bispecific monoclonal antibody, reactive with methotrexate (MTX) and a **tumour** associated **antigen** (gp72) has been produced by fusing spleen cells from MTX **immunised** mice with **791T**/36/3 (anti-gp72) hybridoma. The hybrid antibody was purified from anti-MTX and anti-gp72 antibodies present in the hybridoma culture supernatant by combinations of affinity chromatography on a MTX-agarose immunoabsorbent and stepwise acid elution from Sepharose-Protein A. A particular feature of the present antibody is that it reacts with conjugated MTX; this would allow in vivo targeting of conjugates, increasing many fold the number of molecules of drug carried or localising to pre-targeted antibody. Dual binding between **tumour** cell surface **antigen** and MTX was demonstrated by the ability of the hybrid antibody to bridge between **tumour** cells and MTX as MTX-HSA conjugate, reaction here being detected by flow cytofluorimetry. Purified hybrid antibody specifically enhanced the in vitro cytotoxicity of MTX-HSA for gp72 positive **tumour** cells.

L10 ANSWER 28 OF 38 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 91030518 MEDLINE
DOCUMENT NUMBER: 91030518 PubMed ID: 1699703
TITLE: Application of protein A-rosette assay for screening of monoclonal antibodies to human complement regulatory proteins.
AUTHOR: Seya T; Hara T; Uenaka A; Nakayama E; Akedo H
CORPORATE SOURCE: Department of Immunology, Center for Adult Diseases, Osaka, Japan.
SOURCE: COMPLEMENT AND INFLAMMATION, (1990) 7 (2) 78-89.
Journal code: DOQ; 8903074. ISSN: 1012-8204.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199012
ENTRY DATE: Entered STN: 19910208
Last Updated on STN: 19970203
Entered Medline: 19901207

AB Mice were **immunized** with purified membrane cofactor protein (MCP) and its monoclonal antibodies were screened by protein A(PA)-rosette assay. In this assay, the culture supernatants of hybridoma cells were layered over fixed MCP-bearing cells, and after washing, PA-coated sheep erythrocytes were applied as an indicator to these MCP-bearing cells. No purified antigen was therefore required throughout the screening. More than 300 of the supernatants harvested were successfully examined within 6 h. Each resultant antibody consisted of a single subclass of IgG, and reacted only with MCP in both transblotted and surface-labeled materials. The sensitivity of this assay was then assessed with these purified antibodies. As little as 0.5 micrograms of IgG1 or 0.01 micrograms of IgG2a was found to be detectable with more than 30% rosette formation. There were variations among cell lines in the sensitivity to the PA-rosette assay and the sensitivity did not correlate with the quantity of MCP surface expression in any of the cell lines. K562 gave the lowest background (nonspecific rosette formation) and the best specificity for anti-MCP of the 20 MCP-positive cell lines tested. Cell lines suitable for the detection of monoclonal anti-decay-accelerating factor and anti-C3b/C4b receptor were also examined and CCRF-SB and HSB2, and peripheral blood granulocytes, were found to be proper cell lines for screening the decay-accelerating factor and C3b/C4b receptor, respectively. Clones for anti C3b/C4b receptor were successfully obtained using granulocytes by the PA-rosette assay. This method needs no purified antigen and facilitates the rapid screening and purification of positive clones against cell-surface complement regulatory proteins.

L10 ANSWER 29 OF 38 MEDLINE DUPLICATE 19
ACCESSION NUMBER: 89358089 MEDLINE
DOCUMENT NUMBER: 89358089 PubMed ID: 2788611
TITLE: Human monoclonal anti-idiotypic antibody to the **tumour**-associated antibody **791T**/36.
AUTHOR: Austin E B; Robins R A; Durrant L G; Price M R; Baldwin R W
CORPORATE SOURCE: Cancer Research Campaign Laboratories, University of Nottingham, U.K.
SOURCE: IMMUNOLOGY, (1989 Aug) 67 (4) 525-30.
Journal code: GH7; 0374672. ISSN: 0019-2805.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19891003

AB A human monoclonal antibody, 105AD7, was produced by fusion of a mouse/human heteromyeloma cell line with lymphocytes from a patient previously injected with mouse monoclonal antibody **791T**/36 for **tumour** immunoscintigraphy. The 105AD7 hybridoma has been in continuous culture for more than 12 months, producing a human monoclonal IgG1 which binds to **791T**/36 (IgG2b) and its IgG2a class switch variant, but not a range of other monoclonal mouse immunoglobulins. In quantitative flow cytometric assays, 105AD7 was shown to block the binding of fluorescein-labelled **791T**/36 to its target gp72 **antigen** at the surface of **tumour** cells, but not the binding of 228, an anti-**carcinoembryonic antigen** (CEA) monoclonal antibody to CEA. Tests with purified 105AD7 antibody demonstrated a stoichiometric high-affinity interaction between 105AD7 and **791T**/36. Thus 105AD7 is a human anti-idiotypic antibody which binds at or very close to the binding site of **791T**/36, and as such is a candidate for anti-idiotypic **immunization** of **cancer** patients.

L10 ANSWER 30 OF 38 MEDLINE DUPLICATE 20
ACCESSION NUMBER: 89092468 MEDLINE
DOCUMENT NUMBER: 89092468 PubMed ID: 2783414
TITLE: The influence of syngeneic anti-idiotypic antibody on the biodistribution of an anti-**tumour** monoclonal antibody in BALB/c mice.
AUTHOR: Pimm M V; Durrant L G; Baldwin R W
CORPORATE SOURCE: Cancer Research Campaign Laboratories, University of Nottingham, UK.
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (1989 Jan 15) 43 (1)

147-51.
Journal code: GQU; 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198902
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19890223

AB BALB/c mice were **immunized** against syngeneic murine **791T**/36 monoclonal antibody (MAb) by intraperitoneal (i.p.) injection of the antibody conjugated to ricin toxin A chain. Subsequently, in these and control mice, the biodistribution of radioiodinated **791T**/36 antibody and isotype-matched (IgG2b) control immunoglobulin was examined. Pre-treated mice showed marked perturbation of biodistribution of the **791T**/36 antibody but not of control IgG2b. This was manifest as rapid hepatic clearance of the antibody which was followed by accelerated catabolism and excretion of the radiolabel. Anti-idiotypic antibodies were identified in immunotoxin pretreated mice by their ability to inhibit the binding of FITC-labelled **791T**/36 antibody to **tumour** target cells. These studies show that antibody responses, even to only the idiotype of a MAb, may produce marked perturbation of its biodistribution. This has implications for the clinical use of human or chimeric MAbs for **tumour** imaging or targeting of therapeutic agents since, if anti-idiotypic antibodies are evoked, they could still prevent **tumour** localization of antibody or conjugate.

L10 ANSWER 31 OF 38 CANCERLIT
ACCESSION NUMBER: 87636886 CANCERLIT
DOCUMENT NUMBER: 87636886
TITLE: IMAGING OF BONE AND SOFT TISSUE **TUMORS** USING AN **ANTITUMOR** MONOCLONAL ANTIBODY.
AUTHOR: Armitage N C; Perkins A C; Pimm M V; Baldwin R W; Hardcastle J D
CORPORATE SOURCE: The Univ. of Nottingham, Dept. of Surgery, Floor E, West Block, Univ. Hosp., Nottingham NG7 2UH, UK.
SOURCE: Non-serial, (1986). Nuclear Medicine in Clinical Oncology. Current Status and Future Aspects. Winkler C, ed. New York, Springer-Verlag.
DOCUMENT TYPE: (MEETING PAPER)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 198709

AB In previously reported work, a monoclonal antibody was raised against the human osteosarcoma cell line **791T** and was

demonstrated to show strong reactions with the **immunizing** osteosarcoma cell line and other osteosarcoma cell lines but no reaction with fibroblasts, human red blood cells, or peripheral mononuclear cells. In the present work, imaging of bone and soft tissue **tumors** is reported in 20 patients with proven or suspected **tumors**, using **791T**/36 monoclonal antibody labeled with either 131I or 111In; and imaging of xenografts of osteosarcoma from one of these patients is reported. Positive images at sites of primary **tumors** were given by all five patients with osteosarcomas, by 2/3 patients with malignant fibrous histiocytomas, by a patient with Ewing's sarcoma, by one with a small-cell **tumor** of the chest wall, and by one with an osteoblastoma, but not by one with an osteoclastoma. One of two patients with chondroma gave a positive image, but this chondroma had been traumatized. Three patients with stress fracture were negative as was a patient with Paget's disease, but both of two patients with chronic osteitis gave positive images. In a binding assay using fluorescein isothiocyanate-labeled **791T**/36 antibody with xenograft cultured cells and with **791T** cultured cells, strong binding of **791T**/36 to the cells was observed. This binding was suppressed by addition of increasing concentrations of unlabeled antibody. On injection of 131I-**791T**/36 antibody and 125I-normal mouse Ig into immunodeprived mice bearing xenografts, the antibody level in the xenografted **tumor** was observed to be 2.5 times greater than that of the control IgG2b (**791T**/36 is an IgG2b antibody). This localization was confirmed by gamma camera scintigraphy, which gave clear images of the **tumor** site. (22 Refs)

L10 ANSWER 32 OF 38 MEDLINE DUPLICATE 21

ACCESSION NUMBER: 87158297 MEDLINE
DOCUMENT NUMBER: 87158297 PubMed ID: 3470084
TITLE: Differentiation between monoclonal antibody-defined **antigens** on a human osteogenic sarcoma cell line (**791T**) and **tumor**-localizing properties of the anti-**791T**/36 antibody.
AUTHOR: Dawood F; Embleton M J; Price M R; Pimm M V; Byers V S; Baldwin R W
SOURCE: BRAZILIAN JOURNAL OF MEDICAL AND BIOLOGICAL RESEARCH, (1986) 19 (2) 257-69.
Journal code: BOF; 8112917. ISSN: 0100-879X.
PUB. COUNTRY: Brazil
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198704
ENTRY DATE: Entered STN: 19900303

Last Updated on STN: 19900303
Entered Medline: 19870428

AB Two monoclonal antibodies (anti-**791T**/36 and anti-**791T**/48) prepared against an osteogenic sarcoma cell line (**791T**) following xenogeneic **immunization**, reacted against the **immunizing tumor**, but not against normal cells from the **tumor**-donor, using an indirect 125I-protein A binding assay. Both antibodies cross-reacted with a small number of other osteogenic sarcomas and a few unrelated cell lines from an extensive panel, but the specificity of these cross-reactions was different. Both antibodies were labelled with 125I to detect direct binding to target cells, and the specificity of their reactivity was essentially identical to that observed in the indirect assay. Direct binding of each labelled antibody was inhibited by pretreating target cells with its unlabelled counterpart, but the two antibodies could not inhibit each other. The binding of anti-**791T**/36 was also not inhibited by pretreating the target cells with sera from the 791-T-**tumor** donor, which were shown to contain antibody reacting with the autochthonous **tumor**. It is concluded that **791T** has two distinct **tumor**-associated **antigens** recognized by the monoclonal antibodies, and furthermore that at least one of these **antigens** is independent of those recognized by the patient from which the **tumor** cell line was derived. The efficacy of anti-**791T**/36 antibody labelled with radioactive iodine was demonstrated for localizing **tumor** deposits growing in immunodeprived mice.

L10 ANSWER 33 OF 38 CANCERLIT
ACCESSION NUMBER: 87629555 CANCERLIT
DOCUMENT NUMBER: 87629555
TITLE: DESIGN AND DEVELOPMENT OF DRUG-MONOCLONAL ANTIBODY **791T**/36 CONJUGATE FOR **CANCER** THERAPY.
AUTHOR: Baldwin R W
CORPORATE SOURCE: Univ. of Nottingham, Nottingham, NG7 2RD, England.
SOURCE: Dev Oncol, (1985). Vol. 38, pp. 23-56.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 198703

AB The design and evaluation of drug-antibody conjugates is discussed principally with respect to the application of a monoclonal antibody (MoAb) designated **791T**/36, but the general concepts are applicable to other antibodies to **tumor** cells. MoAb **791T**/36 was produced from a hybridoma obtained following fusion of splenocytes from a mouse **immunized** against cells of a human osteogenic sarcoma (**791T**) and murine myeloma

P3NS1. It reacted with 7/14 osteogenic sarcoma cell lines in a radioimmunoassay, but did not react with normal fibroblast cultures, several of which are derived from donors of positive **tumors**, including the donor of **791T**. Primary and metastatic osteogenic sarcomas also reacted with **791T**/36 antibody, as demonstrated by immunoperoxidase staining of surgically derived **tumor** specimens. The antibody reacted against some unrelated **tumor** cell lines, notably colorectal **carcinomas** (3/5 positive), while with other **tumor** types reactivity was restricted to isolated examples or not detected at all. MoAb **791T**/36 was conjugated with methotrexate (MTX; directly and as MTX-human serum albumin-**791T**/36), daunomycin, and vindesine. In most instances antibody conjugation resulted in considerable less cytotoxicity when compared to the free drug. Furthermore, it is not feasible to introduce many drug residues into an antibody molecule without causing marked reduction in antibody reactivity. Direct conjugation of more than four MTX residues to **791T**/36 antibody could not be achieved without significantly reducing antibody reactivity, whereas at least 6 moles vindesine/mole antibody could be readily introduced without affecting antibody. These investigations established that conjugates with well-defined characteristics can be produced and tested for their in vivo effects on human **tumor** xenografts. Conjugates with vindesine and MTX suppressed growth of osteogenic sarcoma **791T** xenografts, but the true therapeutic potential of these conjugates remains to be established. **791T**/36 antibody radiolabeled with 131-I or 111-In localized in human colorectal and ovarian **tumors** and in osteogenic sarcomas, permitting their detection by gamma camera imaging. These findings indicated that **tumor** tissue targeting, rather than specific **tumor** cell targeting, of **antitumor** agents can be more easily achieved. (22 Refs)

L10 ANSWER 34 OF 38 MEDLINE DUPLICATE 22
ACCESSION NUMBER: 84263515 MEDLINE
DOCUMENT NUMBER: 84263515 PubMed ID: 6589212
TITLE: Analysis of a human osteogenic sarcoma antigen and its expression on various human **tumour** cell lines.
AUTHOR: Campbell D G; Price M R; Baldwin R W
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (1984 Jul 15) 34 (1) 31-7.
Journal code: GQU; 0042124. ISSN: 0020-7136.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198409

Searcher : Shears 308-4994

ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19840904

AB The murine monoclonal antibody **791T**/36 cross-reacts with cells other than the **immunizing** osteogenic sarcoma cell line **791T**, upon which the **791T**/36-defined epitope is expressed on a protein of apparent molecular weight 72,000. An investigation was performed to determine whether the epitope occurred on similar molecules on other cell lines. Radiolabelled immunoprecipitates, prepared with the **791T** /36 antibody, from three osteogenic sarcoma cell lines (2 OS, 788T and 278T), the prostate **carcinoma** EB33 and the colon **carcinoma** HcLo each contained a protein with a molecular weight of 72,000 as the major constituent, together with, in some cases, material of lower molecular weight. This heterogeneity was shown by neuraminidase treatment of the immune precipitates to be due to variations in sialic acid content of the **antigens** since, in five of the six cell lines tested, such treatment produced homogeneous material of apparent molecular weight 55,000. Chymotrypsin treatment of the immune precipitates produced in each instance a major polypeptide of molecular weight 47,000 which displayed no microheterogeneity. Immunoadsorbent-purified **antigen** from **791T** cells was shown to bind strongly to Sepharose-wheat-germ agglutinin and less to Sepharose-concanavalin A, confirming the glycoprotein nature of this **antigen**. These studies demonstrate that molecules expressing the **791T**/36-defined epitopes on different **tumour** cell lines are glycoproteins which display heterogeneity with respect to apparent molecular weight that is attributable to varying degrees of sialylation. No apparent differences were detected in the polypeptide "backbone" of these antigenic molecules.

L10 ANSWER 35 OF 38 CANCERLIT
ACCESSION NUMBER: 85608570 CANCERLIT
DOCUMENT NUMBER: 85608570
TITLE: MONOCLONAL ANTIBODY **791T**/36 FOR **TUMOR** DETECTION AND THERAPY FOR METASTASES.
AUTHOR: Baldwin R W; Pimm M V; Embleton M J; Armitage N M; Farrands P A; Hardcastle J D; Perkins A
CORPORATE SOURCE: Cancer Res. Campaign Labs., Univ. of Nottingham, Nottingham NG7 2RD England.
SOURCE: Non-serial, (1984). Cancer Invasion and Metastasis:Biologic and Therapeutic Aspects. Nicolson GL, Milas L, eds. New York, Raven Press.
DOCUMENT TYPE: (MEETING PAPER)
General Review; (REVIEW)
FILE SEGMENT: ICDB
LANGUAGE: English

ENTRY MONTH: 198505

AB The application of an antihuman **tumor** monoclonal antibody, designated **791T**/36, to the detection of **tumors** and the destruction of metastases is reviewed. This monoclonal antibody (subclass IgG2b) was produced by a hybridoma obtained following fusion of mouse myeloma P3NS1 cells with splenocytes from a mouse that was **immunized** against cells of human osteogenic sarcoma line **791T**. Following injection of 131I-labeled **791T**/36 into CBA mice containing xenografts of the sarcoma, preferential localization was observed in the **tumor**. The simultaneous injection of 131I-labeled antibody and 125I-labeled normal IgG2b into **tumor**-bearing mice made it possible to calculate the extent of specific:nonspecific binding of immunoglobulins. Clinical trials designed to establish the localization characteristics of **791T**/36 monoclonal antibody have been conducted so far with osteogenic sarcoma, colorectal **carcinoma**, and ovarian **tumors**. Studies with colorectal **cancer** patients (pts) showed that imaging following infusion of 131I-labeled **791T**/36 antibody was able to detect metastatic **tumors**. A single brain metastasis measuring 2 x 2 x 1 cm was the smallest **tumor** detected to date. Trials in mice have been started to determine the in vivo effectiveness of conjugates of the Vinca alkaloid analogue vindesine (VDS) with **791T**/36 antibody. Initial trials showed that, when treated with VDS-791/36 antibody conjugate at doses equivalent to 19.2 mg VDS and 500 mg antibody/kg body wt, osteogenic sarcoma **tumor** growth was markedly suppressed compared to untreated controls. The conjugates were nontoxic in this regime. Although free VDS produced greater inhibition of **tumor** growth, the dose required exceeded that which was tolerated, resulting in death in 2/6 mice. (35 Refs)

L10 ANSWER 36 OF 38 MEDLINE DUPLICATE 23

ACCESSION NUMBER: 83048824 MEDLINE

DOCUMENT NUMBER: 83048824 PubMed ID: 6958308

TITLE: Complement-dependent cytotoxicity of anti-human osteogenic sarcoma monoclonal antibodies.

AUTHOR: Price M R; Pimm M V; Baldwin R W

SOURCE: BRITISH JOURNAL OF CANCER, (1982 Oct) 46 (4) 601-10. Journal code: AV4; 0370635. ISSN: 0007-0920.

PUB. COUNTRY: ENGLAND: United Kingdom

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198301

ENTRY DATE: Entered STN: 19900317

Last Updated on STN: 19900317

Entered Medline: 19830107

Searcher : Shears 308-4994

AB Two mouse monoclonal antibodies against the human osteogenic sarcoma **791T** were examined for their capacity to exert complement-dependent cytotoxicity against a panel of human **tumour** cell lines. Cytotoxicity was most evident against the **immunizing tumour 791T** although significant reactivity was directed against other osteogenic sarcomas. In admixture, the 2 antibodies displayed synergism in their cytotoxicity although this was only demonstrable with defined ranges of antibody concentration. The cytotoxicity of these antibodies was dependent upon the use of rabbit serum as complement and no **tumour**-cell lysis was produced using human, guinea-pig or mouse serum complement. The more potent cytotoxic antibody failed to modify the outgrowth of **791T** **tumour** xenografts in immunodeprived mice even though localization of antibody at the **tumour** site has been demonstrated (Pimm et al., 1982).

L10 ANSWER 37 OF 38 CANCERLIT
ACCESSION NUMBER: 82605125 CANCERLIT
DOCUMENT NUMBER: 82605125
TITLE: ANTIGENS ON NATURALLY OCCURRING ANIMAL AND HUMAN **TUMORS** DETECTED BY MONOCLONAL ANTIBODIES.
AUTHOR: Embleton M J; Gunn B; Byers V S; Baldwin R W; Bonavida B; Martin W J; Ferrone S
CORPORATE SOURCE: Cancer Res. Campaign Lab., Univ. Nottingham, Nottingham, NG7.2RD, England.
SOURCE: Transplant Proc, (1981). Vol. 13, No. 4, pp. 1966-1969.
ISSN: 0041-1345.
DOCUMENT TYPE: (MEETING PAPER)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 198203

AB Reactivities of monoclonal antibodies prepared against a spontaneously arising rat mammary **carcinoma** and human osteogenic sarcoma cells were studied. An antibody-secreting hybridoma was prepared by fusion of the mouse myeloma P3-NS1-Ag4 (P3NS1) with spleen cells from rats **immunized** against a syngeneic mammary **carcinoma**, Sp4. The monoclonal antibody produced reacted only with mammary **carcinoma** Sp4 and did not bind to other rat **tumors** or normal rat cells. Two cell lines (**791T**/36 and **791T**/48) from hybridomas obtained by the fusion of spleen cells from BALB/c mice **immunized** with the **791T** osteogenic sarcoma cell line with P3NS1 cells, produced antibody that reacted preferentially with **791T** cells. Antibody **791T**/36 reacted strongly with **791T** cells and with another osteogenic sarcoma, 788T, and more weakly with two others, 805T and 845T; the

antibody did not react with six other osteogenic sarcomas. Tests against 11 lines of cultured fibroblasts, including 3 lines derived from the donor of **791T** and 2 from donors of cross-reactive sarcomas, were negative. Monoclonal antibody from **791T**/48 gave different cross-reactions. Two different monoclonal antibodies to a human osteogenic sarcoma cell line reacted with the **immunizing** cell line but not with cultured fibroblasts from the **tumor** host. Neither showed specificities for blood group or D-locus **antigens**. Despite apparent **tumor** association, the **antigens** detected by the monoclonal antibodies were not shared by all osteogenic sarcomas and were not restricted to this **tumor** type. (10 Refs)

L10 ANSWER 38 OF 38 MEDLINE DUPLICATE 24
ACCESSION NUMBER: 81232624 MEDLINE
DOCUMENT NUMBER: 81232624 PubMed ID: 6941806
TITLE: **Antitumour** reactions of monoclonal antibody against a human osteogenic-sarcoma cell line.
AUTHOR: Embleton M J; Gunn B; Byers V S; Baldwin R W
SOURCE: BRITISH JOURNAL OF CANCER, (1981 May) 43 (5) 582-7. Journal code: AV4; 0370635. ISSN: 0007-0920.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198109
ENTRY DATE: Entered STN: 19900316
Last Updated on STN: 19900316
Entered Medline: 19810915

AB Monoclonal antibody against an osteogenic-sarcoma cell line (**791T**) was prepared by production and cloning of a somatic-cell hybrid between the mouse myeloma P3-NS1 and spleen cells from **791T-immunized** mice. Three clones of hybridoma producing antibody against **791T**, as detected by 125I-labelled Protein A binding, were tested against a range of normal and **tumour** cell targets to determine the pattern of expression of the **antigen** detected. The 3 clones had identical activity. They reacted strongly against **791T** cells and another osteogenic sarcoma, 788T, and more weakly against a further 2 from a total panel of 10 osteogenic-sarcoma lines. The antibody was negative for fibroblasts from the donor of **791T** , and for other fibroblasts, human red blood cells, human peripheral mononuclear cells and sheep red blood cells. When tested against a panel of unrelated **tumours**, they reacted against individual cell lines derived from **carcinomas** of colon, lung, bladder and cervix. These cross-reactions were not observed with other colon or lung **carcinomas**, and it is suggested that the antibody was reacting with a **tumour**-associated

antigen expressed randomly on different **tumour**
types, rather than specifically on osteogenic sarcomas.

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